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ABSTRACT

Intended for parents and professionals, the book explains chromosome abnormalities in lay terms and discusses the relationship of specific conditions to birth defects. Chromosomal abnormalities are defined and factors in diagnosis and recurrence are discussed. Normal chromosome reproduction processes are covered while such numerical abnormalities as mosaicism and such structural defects as deletions, translocations, and inversions are explained. Diagnosis, especially prenatal detection, is considered in detail. The final section relates chromosome abnormalities to a range of difficulties associated with birth defects. Resources (volunteer, parent, and information agencies) are discussed. The book concludes with photographs of children with chromosome abnormalities and excerpts of interviews with parents. (CL)

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AUTOSOMAL CHROMOSOME ABNORMALITY

A Cause of Birth Defects

A book written for parents and professionals explaining chromosome abnormalities in lay terms and discussing how these specific conditions relate to the more common problem of birth defects.

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Genetics Clinic
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Photography by Douglas Hepburn

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AUTOSOMAL CHROMOSOME ABNORMALITY

A Cause of Birth Defects

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INTRODUCTION

Birth defects are common. This tragedy occurs in about three percent of all births and defects can range in degree of complexity from mild to severe. Autosomal chromosome abnormalities* are only one cause of birth defects. Abnormalities of any one specific chromosome (except for the numer 21) are rare. However, when the total defects due to all chromosome errors are combined, they are not rare. The frequency of a major chromosome abnormality is found in between one in every one hundred and fifty and two hundred births, and it is estimated that as many as one in every twenty conceptions may contain a chromosome error.[7]

There is little literature available to the layman dealing with chromosome errors, or explaining how patients with these problems are different, yet are similar to patients with other multihandicapping conditions. Therefore, this book has been written both for parents who have had a child born with an autosomal chromosome abnormality which has resulted in a recognizable birth defect and for the nurses, educators, social workers and counselors who are there to help them.

There are no easy answers to the universal questions "What is wrong?"; "How did it happen?"; "What can we do?"; and "Will it happen again?" Genetics clinics, such as that of Crippled Children's Division at the University of Oregon Health Sciences Center are now addressing specific questions unique to families with a chromosome disorder. By doing this it is

*Underlined words will be found in the glossary at the back of the book.

hoped that the causes and results of chromosome disorders will be removed from the realm of mystery faced by any family who has had a child born with a major birth defect.

This book has been divided into three parts. Part I discusses chromosomes and chromosome errors. Part II answers the questions families frequently ask regarding the diagnosis, (recognition of the problem,) prognosis, (probable expectations regarding the problem,) and recurrence, (will it happen again?). Part III not only places chromosome abnormalities in the broader range of birth defects, but offers general help to any family with a birth defect seeking information about where to turn for assistance. It also shares some experiences of families who have children with autosomal chromosome abnormalities. Because of the infinite variety of chromosome errors, specific problems relating to individual chromosomes are not discussed here. A general framework is instead given, allowing the family's geneticist or counselor to fill in the details giving answers to specific questions posed by their own particular situation. Health professionals can use this book not only for their own information but as a guide for counseling families.

We do not pretend to have all the answers and we have no magic cures. In approaching the specific problem of any given child, it takes the integrated effort of the family, counselors and geneticists working as a team to arrive at a positive solution to a difficult problem.

CHAPTER I

PRELIMINARY QUESTIONS REGARDING THE DIAGNOSIS

Quote: "In this I have no regrets. She was a wanted baby and conceived in love. I can feel no guilt that she was not born perfect."

Most families desire as much information as possible about their child's problem. By pursuing it, they eventually become sophisticated in their knowledge of their child's condition. However, medical terminology is often foreign to them at first exposure, and it takes time and repetition for a parent to develop a sense of comfort in dealing with new and emotionally laden material. Often parents, at the time their baby is born with a chromosomal birth defect, have only a vague idea of what the doctor is saying. Terms, such as chromosomes, genes, cells, congenital and hereditary are only vague memories from half-forgotten biology courses.

Thus, one of the first, but most important aspects of discussing a child's problem with a family lies in the agreed upon understanding of words, thereby making sure that everyone is using and understanding the same vocabulary. For instance, in these days of popular medical writing many words are used interchangeably, but with subtle variations of meaning. A primary example is the variation in the use of the genetics. In general terms, human genetics is the study of those traits, good and bad, that are passed on from parents to children through succeeding generations. In precise terms, genetics is the branch of

biology that deals with heredity and medical genetics is the branch of medicine that deals with disorders that are inherited. Genetic diseases are abnormalities caused by single genes, several genes, or by an excess, deficiency or rearrangement of the chromosomes* which contain a large number of genes.

Single gene defects are inherited and can be passed on from parent to child in what are called Mendelian inheritance patterns, named after the Austrian monk Gregor Mendel who first observed and recorded these laws of inheritance. Some conditions are called polygenic, meaning many genes are involved to create a change, a change which may be either good or bad. Some conditions are considered to be multifactorial, meaning many factors are involved; use of this term means the environment, as well as the genes, play a part in the development of a trait or disorder.

For those families with a child with an identified genetic defect, genetic counseling is, in precise terms, the communication process that takes place between parents and physicians regarding the specific problems due to the diagnosed disorder in their child, the prognosis for the current child, as well as the recurrence risk for having another similarly affected child. In broader terms it also covers the practical factors of medical management for the child and gives support to the family's emotional, psychological and general health needs caused by the extraordinary impact of the child's defect on the family.

*See Chapter II, paragraphs "Genes" and "Chromosomes" for a more complete discussion.

What is a Chromosome Abnormality?

Chromosomes are thin thread-like fibers of material which contain the genes. They are found in the nucleus of each cell. It is the genes which give each person his or her individual and hereditary characteristics.

Chromosome errors, either in number or structure, generally occur during, or prior to, conception. Errors may happen in the individual sperm or egg or in the fertilized egg itself, resulting in either too much or not enough genetic material. Consequently, the baby may be born with several birth defects ranging from minor to severe.

The primary thing to remember regarding chromosome disorders is that CHROMOSOME ABNORMALITIES INVOLVE ERRORS IN THE GENETIC MATERIAL, BUT THEY ARE NOT NECESSARILY INHERITED BY BEING PASSED FROM PARENT TO CHILD.

THERE IS NO FAULT INVOLVED IN THE CONCEPTION AND BIRTH OF A BABY WITH A CHROMOSOME ERROR. As far as medical science knows, nothing in the mother's or father's diet, activity or emotional experiences causes the chromosome error. Since the chromosomal mistake happened either in the development of the sperm or the egg prior to, at, or just after conception, a parent has no prior knowledge or control over this happening. Even in families in which a balanced translocation is segregating through the family, it is usually the birth of a first affected child that signals this event. It is only then that families can be forewarned regarding subsequent pregnancies.*

*See Chapter III, paragraph "Translocations."

What Makes the Doctor Suspect A Chromosome Abnormality?

The primary concern about the baby may be obvious physical problems such as a cleft lip, a skeletal deformity or a heart murmur. Or, the problem may be more subtle, such as a general laxness of muscle tone and a hard to define "look" which the doctor may call dysmorphic. It is often a combination of such concerns that causes the doctor to request a chromosome study.

In general, a karyotype* is done for diagnosis when a child has multiple congenital anomalies and mental retardation. (Even though it is not always readily apparent in the early weeks or months of life, mental retardation is the one most consistent feature of chromosome abnormalities.) Since birth there have been several physical and/or developmental problems which may be accompanied by dysmorphic features.

Dysmorphic features are created by a collection of subtle differences most readily seen in the face, hands and feet. They are often found in the general population, and when one or two unusual features are seen in an otherwise healthy person, they can be insignificant and considered a variation of normal. However, even though the dysmorphic features themselves are apparently insignificant such things as wide-spaced eyes, low-set and/or abnormally shaped ears and fingers which are short and stubby or very long and slender, can be clues to a discerning eye which knows that these little external signs are associated with more severe and complex internal problems.**

*See Chapter II, paragraph "Chromosomes."

**See Chatper IV, paragraph "Physical Examination."

How Rare are Chromosome Disorders?

Chromosome abnormalities collectively are not rare. They only give the impression of being rare. Until recently the bulk of childhood diseases were problems caused by communicable diseases and faulty nutrition. As these problems have become documented and controlled, many previously undiagnosed conditions are now being found to be chromosomal in origin.

We now know that an estimated one out of every 150-200 births results in a child with a significant chromosome abnormality. As a result, due to this cause, 15-20 million Americans are born each year with major handicapping conditions.[7]

About 36% of all recognized spontaneous abortions (more than 100,000 per year in the United States) are caused by gross chromosome abnormalities.[23] This does not take into account the many thousands of early miscarriages that take place prior to the mother realizing that she is pregnant or the fact that the fertility of the egg or sperm itself may be affected, resulting in a nonviable conception. Spontaneous abortions are nature's way of protecting us from even more serious birth defects. Only those fetuses with errors which are compatible with life survive to term, although many which can survive in the protection of the womb are not compatible with a long and healthy life in the external world.

Will It Happen Again?

This is a difficult question to answer and is dependent upon the type of error and the family history. There are no really precise recurrence risks for any chromosome condition, except for the classic chromosome error resulting in Down's Syndrome.

The recurrence risk for Trisomy 21, or Down's Syndrome (previously known as mongolism), the most common autosomal chromosome abnormality, is well established. It is also known that the incidence of this abnormality rises with increased maternal age. The risk rises significantly for mothers over the age of 35 and increases sharply after age 40. The risk of occurrence related to maternal age is shown in the table below.

Mother's Age	Risk of Down's Syndrome[22]
Under 19	About one in 2,300
20-25	1,600
25-30	1,200
30-35	880
35-40	290
40-44	100
Over 45	46

If a mother gives birth to a Down's child, there is a chance in risk for another child being born with Down's to a one to three percent. The why's of this are not yet known.*

In rare chromosome abnormalities, a rule of thumb is that the more rare the error, the more unlikely the recurrence IF IT IS NOT DUE TO A FAMILIAL TRANSLOCATION. The figures for each individual abnormality are too low to give a valid assumption; however, the risk is clearly low, surely less than 1%. Since one of the primary purposes of genetic counseling is to establish and give a recurrence risk figure to a family regarding subsequent

*See Chapter III, paragraph "Nondisjunction."

pregnancies, this imprecise answer is vague and frustrating. One of the primary thrusts in research is to try to obtain information which will give families a more definitive answer to this question.*

The one available technique for determining if a current pregnancy is similarly affected is through prenatal diagnosis. Prenatal diagnosis can reveal the presence of abnormal chromosomes in a fetus before its birth, giving parents an option to terminate or continue the pregnancy as they desire.**

*See Chapter V, paragraph "Research."

**See Chapter VI, paragraph "Prenatal Diagnosis."

CHAPTER II

NORMAL CHROMOSOME REPRODUCTION

Quote: "Most people walking around don't know about chromosomes. They don't even know that they have 46. It takes a long time to understand."

To better understand what has happened to a chromosomally defective baby, it is best to have an understanding of how cells normally develop, how chromosomes function and how sex cells, eggs or sperm, divide before uniting at conception to form a new baby. Nature has a master plan. There is a basic logic and design to life marvelously simple and complex so that when all of the steps are accurately followed, a unique and perfect human being is created.

Cells

The body is made up of billions of cells which are individual masses of protoplasm, masses of living material, held together with a thin skin called a cell membrane. These cells can be seen through use of a microscope.

In the middle of each cell is the nucleus, surrounded by the nuclear membrane, which contains the chromosomes and which acts as the control center for the specific function of that particular cell. All cells have a similar structure even though they have a variety of purposes. It is the nucleus which tells the cell what kind it is going to be and what it is going to do. Some cells make up the skeletal system, some the internal organs, others the brain and skin and so forth. Except for nerve cells, cells constantly multiply, divide and die at a variety of rates

depending upon their purpose and function. It is estimated that in the human body during every second of its life 50 million cells are dying while 50 million others are being replaced.

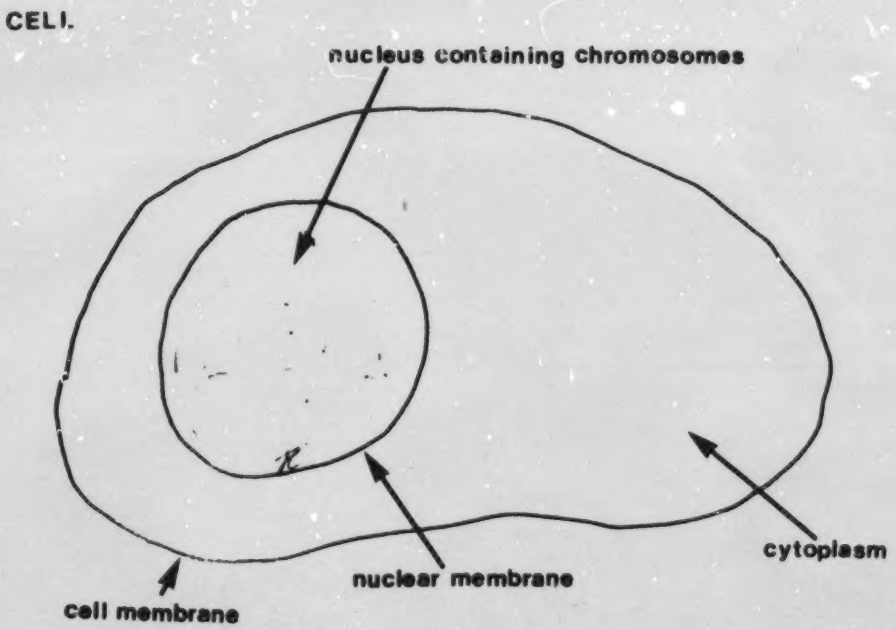


Figure 1. A CELL The basic structure of each cell is similar. It is the nucleus within the center of each cell which acts as the control center for the specific function of that cell. Within the nucleus are the chromosomes composed of individual genes, which in turn are made up of long chemical chains of deoxyribonucleic acid, or DNA. It is this genetic material found in the chromosomes within the nucleus which gives each human being his or her specific characteristics.

Genes

Chromosomes found in the nucleus of the cell are made up of long chemical chains called deoxyribonucleic acid or DNA. Genes are specific subunits of DNA. This genetic material of the chromosomes is what is passed on to our offspring, giving each human being his or her specific characteristics such as

eye color, skin pigment, blood type and so forth. While chromosomes can be seen, genes are so small they cannot be seen even with a microscope.

Although it has been estimated that there are somewhere between 10,000 and 100,000 genes in EACH cell, as yet the exact chromosomal location of only 200 plus genes is known, while there is some information regarding 1,000 or more.

The genes and chromosomes in the body can be compared to a very long and complex novel. In this context a gene can be thought of as a single letter and the DNA as a word. One chromosome would constitute one sentence and one cell a chapter. So it is with our bodies. Our heredity is basically constructed from a handful of chemicals just as a novel is created from the 26 letters of the alphabet. It is in the unique arrangement and composition of the genes that our total body story is told.

Chromosomes

Chromosomes are found in all body cells except for mature red cells. Within the nucleus of each of the cells are 23 matching pair of chromosomes, called homologues, or 46 total chromosomes, one half of the 46 coming from our mother and one half of the 46 coming from our father. We inherit 25% of our genetic material from each grandparent with this division continuing back into time. In turn, we pass on one half of our genetic material, 23 chromosomes, to our children with the other half coming from our partner.

When new cells are made, each chromosome goes through a process of making a copy of itself and then splitting in half lengthwise; the cell then divides with each chromosome half going

into a new cell. This process, called mitosis, is similar in all living organisms and continues as long as the organism lives in all dividing cells except for the egg and sperm.

To observe this mitotic process, cells must be obtained from a sample of body tissue such as blood, bone marrow or skin. Usually a blood sample is taken from the arm as this is the best procedure, being easy, economical and almost painless. The cells are then grown in a culture, subsequently strained and then photographed in a cytogenetics laboratory.*

It is at a stage of chromosome division called metaphase that the chromosomes are most easily studied in the laboratory since the individual features are most clearly observable at this point. Under the microscope the chromosomes seen on the slide appear to be short and puffy, just about to divide into two chromosomes, but still held together at the middle, or centromere. It is at this point that any abnormal or unusual features can be easily distinguished. Next the chromosomes on the slide are stained, photographed, enlarged, cut out and then arranged into a specific pattern on a sheet of paper. This pattern is one which has been agreed upon by all the cytogenetics labs in the world. The photograph of this pattern of chromosomes arranged on a sheet of paper according to their size, position of centromere and arrangement of bands is referred to as the karyotype.

*See Chapter IV, paragraph "How Are Chromosomes Studied?"

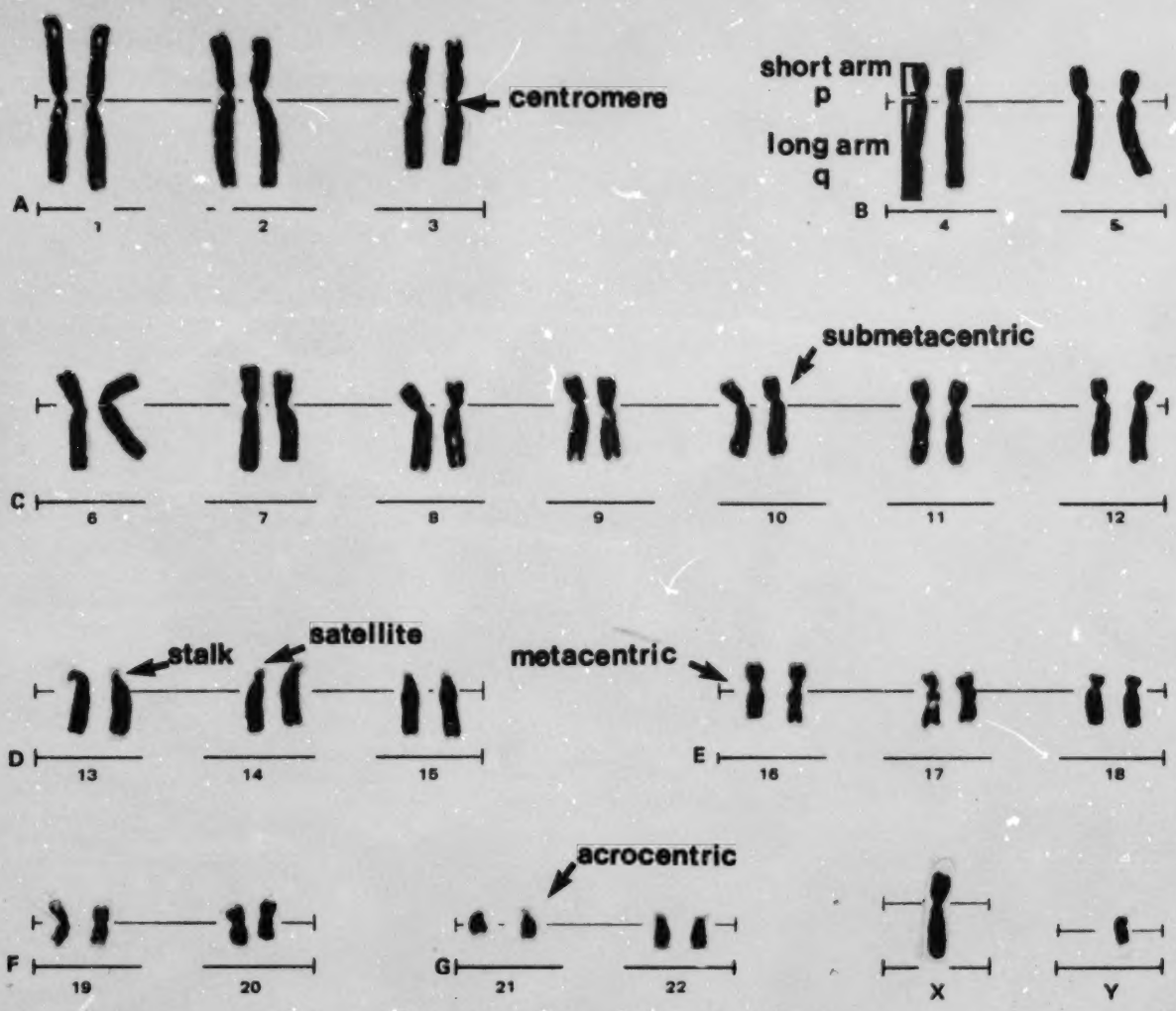
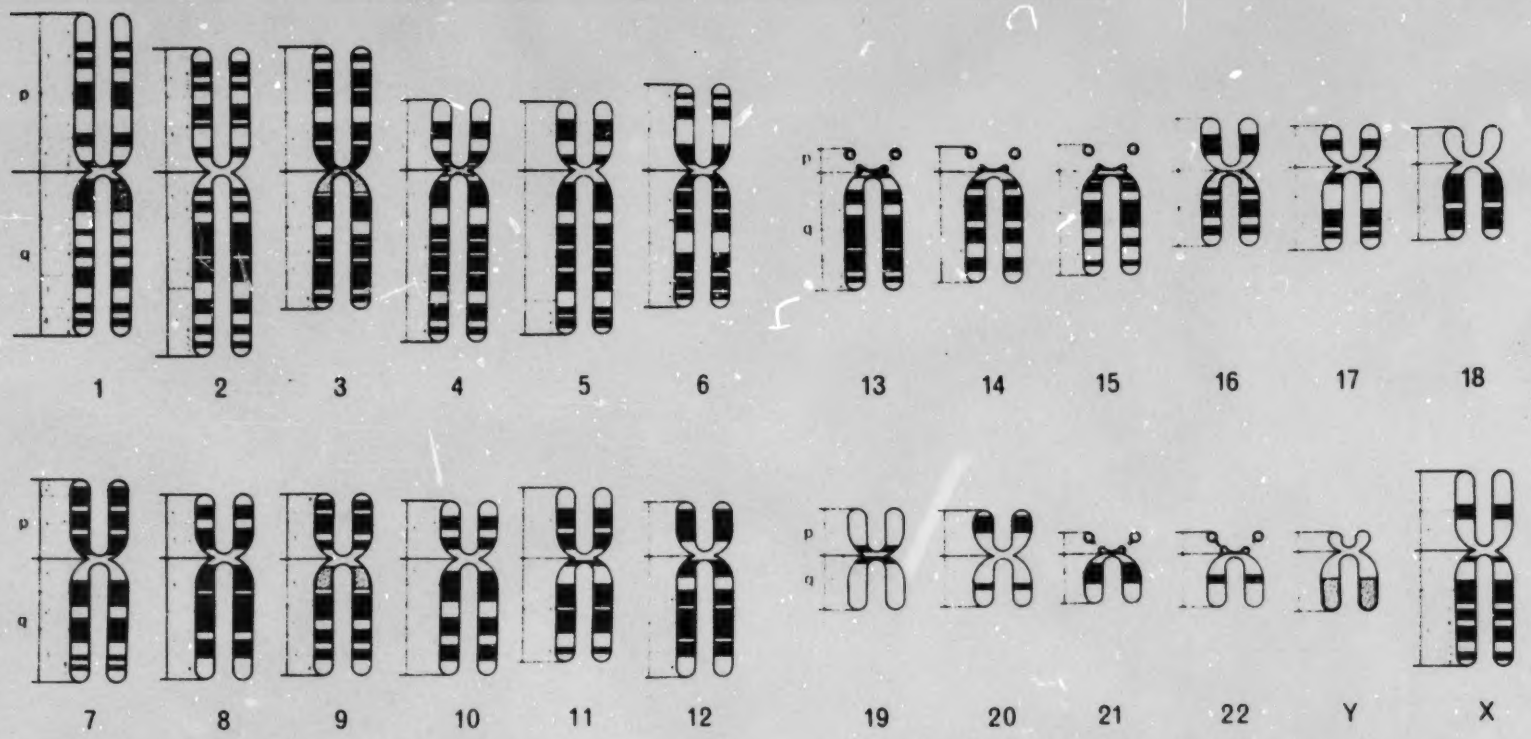


Figure 2. CHROMOSOME NOMENCLATURE The various sections of the chromosomes have specific names. The point where the chromosomes are joined together, just prior to splitting, is called the centromere. The correct name for the top half of the chromosome is the short arm, or the p segment. The correct name for the bottom half of the chromosome is the long arm, or the q segment. The centromere may be located anywhere along the chromosome. If it is in the middle and the top and bottom halves are about the same length, it is referred to as a metacentric chromosome. If there is a distinct difference and the top half is clearly shorter than the bottom half, it is referred to as a submetacentric chromosome; if there is very little material at the top, it is called an acrocentric chromosome. Acrocentric chromosomes often have what appears to be a little space above the chromosome topped with small dots. Actually there is no space; this area does not stain readily, but does contain DNA. The so-called space is referred to as the stalk and the little dots are called the satellites.

The light and dark bands seen on the chromosomes are not the genes. By using various procedures and stains it is possible to make the bands appear in varying shades of light and dark. These patterns of light and dark on each chromosome are consistent in all humans. The common laboratory expression for the procedure used in the uncovering of the bands is called a banding technique* and the design of bands found on each chromosome is called the banding pattern. The most commonly used stain is Giemsa; it shows the chromosomes' individual characteristics most easily.

Each band has been given an arbitrary number and universally a specific set of numbers refers to the same section of chromosome in any laboratory. Within the bands there are subnumbers which increase as new bands are discovered. As new bands continue to be identified, there are regularly scheduled national and world wide meetings to keep the numbers updated and the information uniform and consistent.**

*See Chapter IV, paragraph "Staining Techniques."
**See Chapter IV, paragraph "Elongated Chromosomes."



Negative or pale staining Q and G bands Positive R bands

Positive Q and G bands Negative R bands

Variable bands

Figure 3. IDEOGRAM A stylized standardization of human chromosomes, called an ideogram was developed in Paris in 1970 and published in 1971. This is still the most common karyotype diagram used by cytogenetic laboratories today. The arms are clearly defined as p and q; each arm is divided into numbers and the bands into subnumbers. As more bands are uncovered the numbering system can be reduced into further subunits. Paris Conference (1971)

14

23

22

Meiosis

Each normal cell nucleus has 22 distinct pairs of chromosomes called autosomes in addition to a pair of sex chromosomes designated as XX for a female and XY to a male. This makes a total of 23 pair, or 46 chromosomes, in each cell. Under usual conditions the female ovum, or egg, has 22 autosomes and one X, or sex, chromosome. The male sperm cell has 22 autosomes and either an X or a Y chromosome. Therefore, the genetic difference between men and women lies in these sex chromosomes. It then follows that if the sperm with an X joins with the cell of the woman, a girl is conceived; if a sperm with a Y joins, a boy is conceived. Upon conception the fertilized egg, (referred to as a zygote for the first ten days of gestation), starts immediately to divide by the process of mitosis and quickly becomes the millions of cells necessary to produce a new baby.

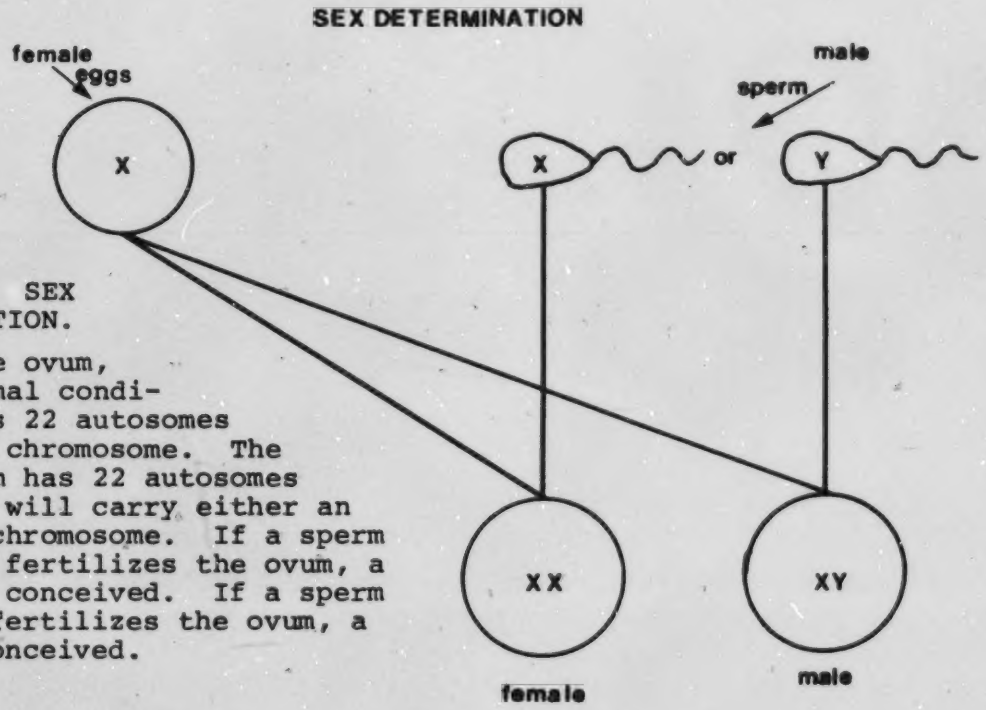


Figure 4. SEX DETERMINATION.
The female ovum, under normal conditions, has 22 autosomes and one X chromosome. The male sperm has 22 autosomes also, but will carry either an X or a Y chromosome. If a sperm with an X fertilizes the ovum, a female is conceived. If a sperm with a Y fertilizes the ovum, a male is conceived.

GENETICS CONSULTATION
LABORATORY REPORT

Unit No.
Name
Birthdate

46,XX

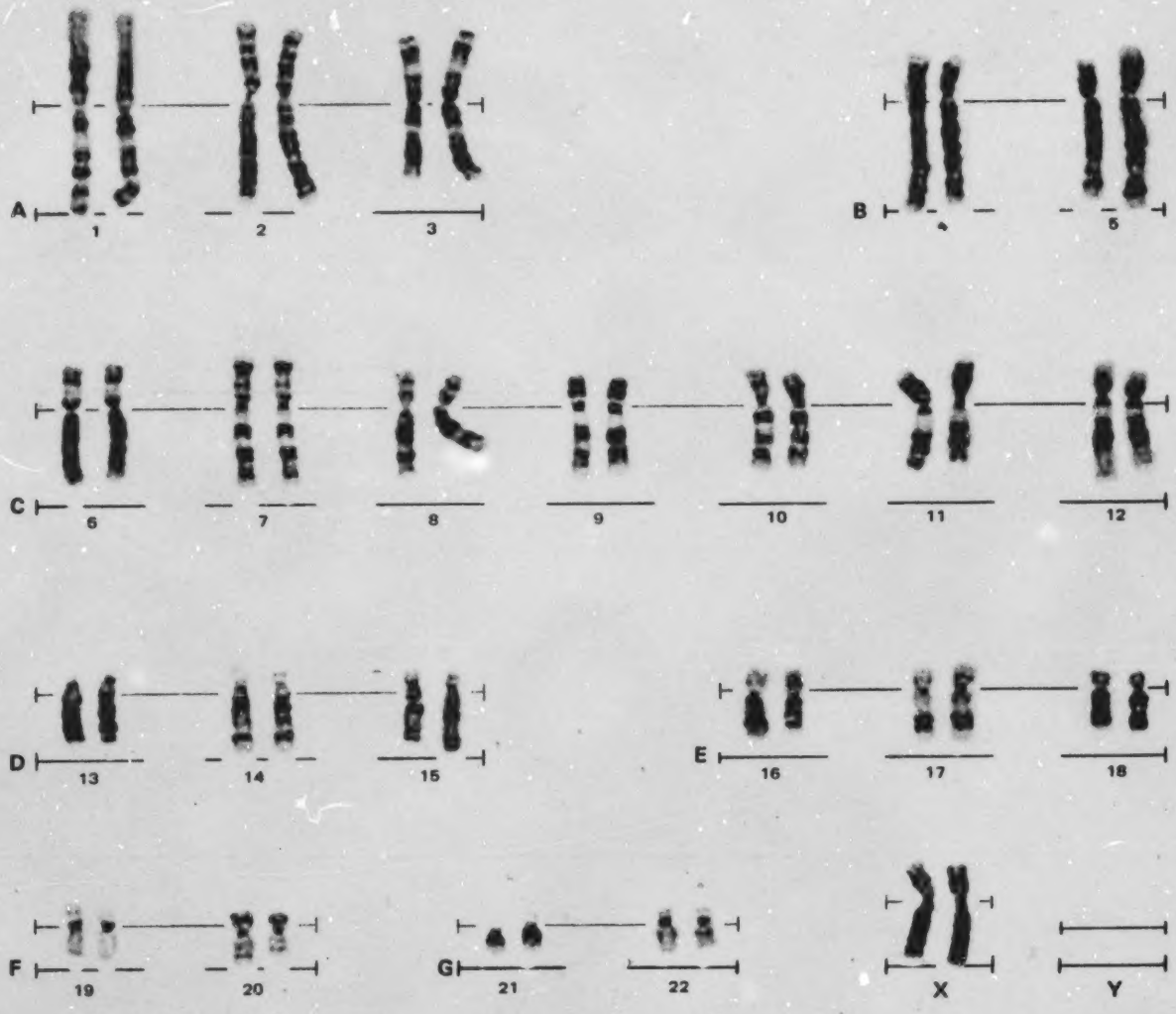


Figure 5. FEMALE KARYOTYPE (Giemsa banded) The paired autosomes of the male and the female are not recognizably different. The two X chromosomes indicate this is the karyotype of a female.

GENETICS CONSULTATION
LABORATORY REPORT

Unit No.
Name
Birthdate

46,XY

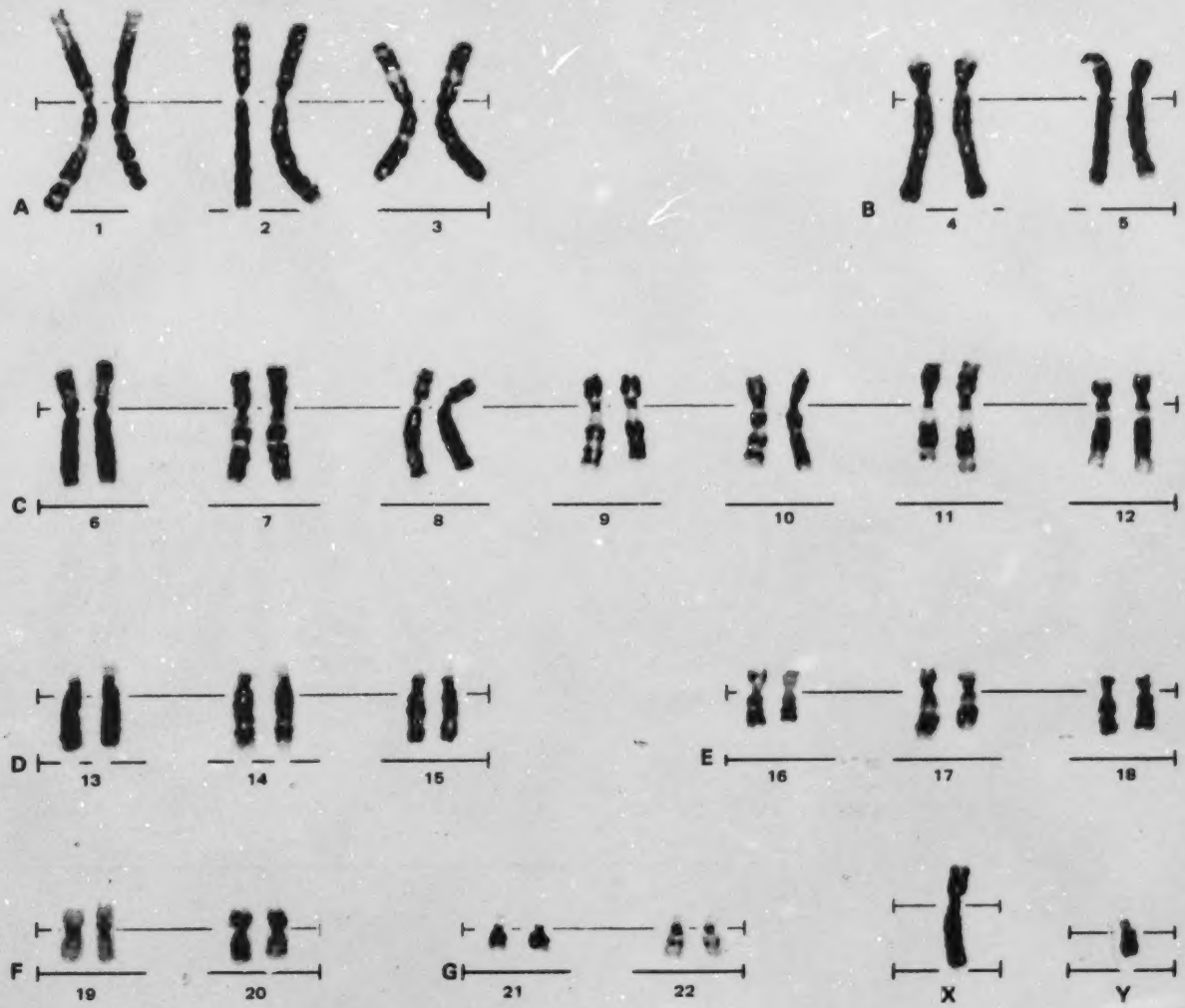


Figure 6. MALE KARYOTYPE (Giemsa banded) It is the one X and the one Y chromosome that indicate this to be the karyotype of a male.

In the reproduction process it is obvious that a cell with 46 chromosomes cannot unite with a cell with 46 chromosomes and produce another normal cell with 46 chromosomes. If this happened, the cells would each have 92 chromosomes at the first division and cellular chaos would, and occasionally does, occur. Therefore, normal 46 count cells have to reduce to 23 count cells so when united, the proper complement of 46 is obtained. To accomplish this, these 23 count cells called gametes are produced through a two-step reduction called meiosis.

Meiosis is divided into two steps called meiosis I and meiosis II. In a woman, part of meiosis I occurs prior to her birth. A woman has all of her egg cells in the ovaries about three months before she is born. The eggs have partially completed the first stage of meiosis I and the eggs remain arrested in this state until ovulation which occurs monthly between approximately 13 to 50 years of age. It is just prior to the releasing of the egg at the time of ovulation that meiosis I is completed; meiosis II is completed after fertilization.

In contrast, the production of male sperm follows a much more dynamic process and spermiogenesis goes on continually from puberty. Since male sperm are made fresh about every six weeks, the states of meiosis I and II come close together.

One half of each pair of the chromosomes comes from the mother and one half from the father, each with different genetic information. Chromosomes from the mother are referred to as maternal chromosomes and from the father as paternal chromosomes. To assure that there is a thorough mix between the maternal and paternal genetic information prior to conception, both the egg

and the sperm undergo two significant occurrences in meiosis, crossing over and random segregation.

It is continual crossing over and random segregation occurring in the reassortment of maternal and paternal material in both the egg and sperm prior to fertilization that results in the remarkable difference in siblings. The details of the process, what occurs and when, are still open to debate and investigation, but basically the ultimate gametes which enter into the fertilization process are a combination of thousands of genes which have been carried forward from grandparents and great-grandparents on both sides of the family going back into antiquity. It is this exquisite variety of recombination that allows each of us to be totally unique.

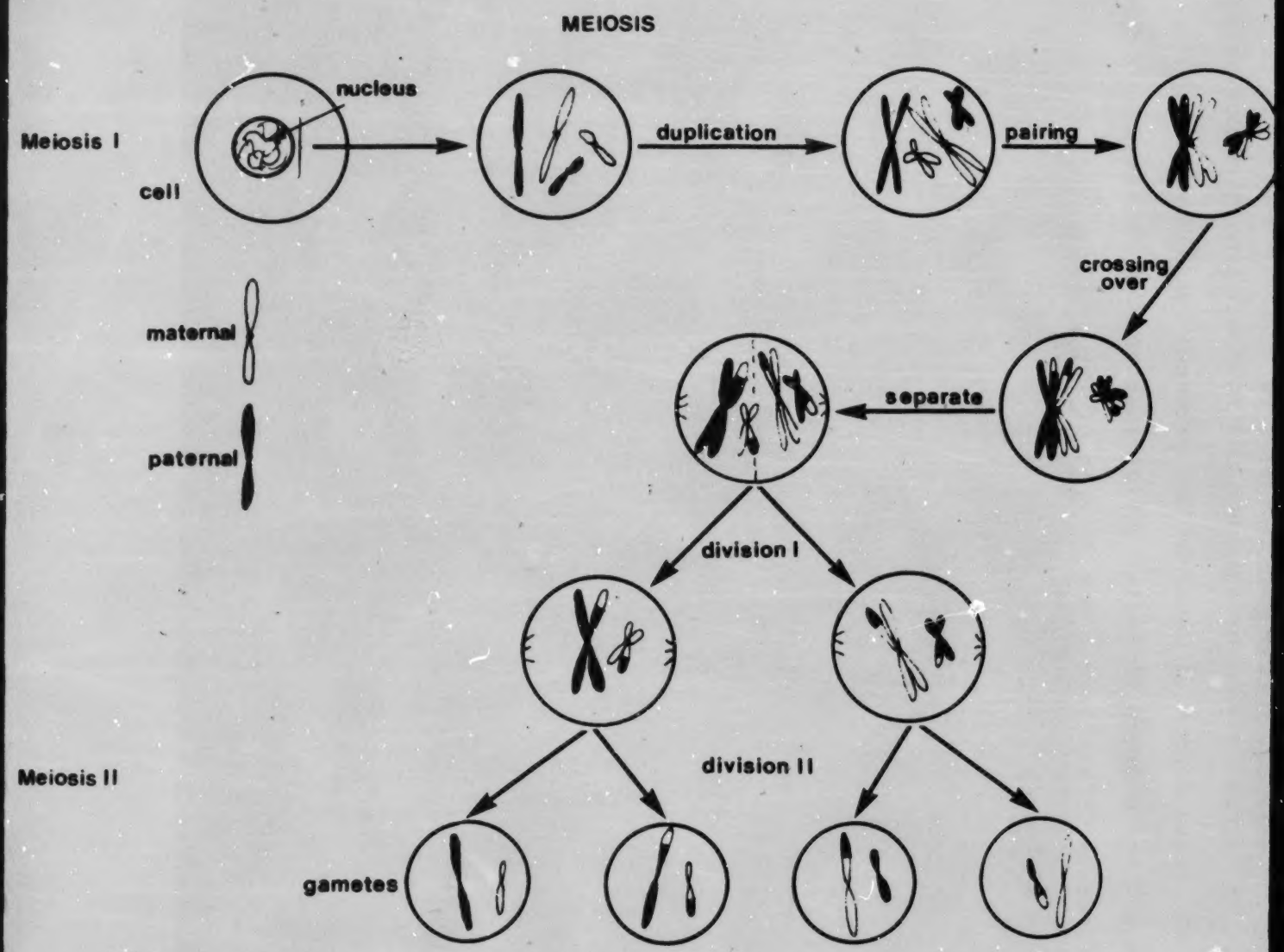

MEIOSIS
Meiosis I
cell
nucleus
duplication
pairing
crossing over
maternal
paternal
separate
division I
Meiosis II
division II
gametes

Figure 7. MEIOSIS For simplicity, only two maternal and two paternal chromosomes are represented in this diagram. Meiosis follows a logical sequence.

Meiosis I

1. Each chromosome of the 23 pairs duplicates itself, sharing the same centromere. These duplicated chromosomes then match up intimately with their partners, much like a zipper. At some points, they CROSS OVER each other and exchange material, thereby mixing up some of the maternal and some of the paternal chromosome material.

2. The maternal chromosome next separates longitudinally from the paternal chromosome, each with its exchanged material going to different ends of the cell.

3. The cell itself now begins to divide and only one partner of each of the chromosome pairs goes into each new cell. These new cells are called daughter cells. There is a 50/50 chance as to whether the maternal or paternal chromosome goes into each cell. This 50% chance is what is referred to as RANDOM SEGREGATION. Meiosis I ends with 23 duplicated chromosomes in each cell instead of 46.

Meiosis II

1. The duplicated chromosome splits in half longitudinally at the centromere, each half again randomly going to one of two new daughter cells.

2. At the conclusion of meiosis I and meiosis II, there are four daughter cells with one copy of each chromosome in each cell equaling 23 individual chromosomes per cell.

In the male, all four cells, now called gametes, remain functional, but in the woman only one gamete remains functional while the other three, for reasons still unknown, degenerate and disappear.

At this point, the egg and sperm are ready for uniting to create a new human being.

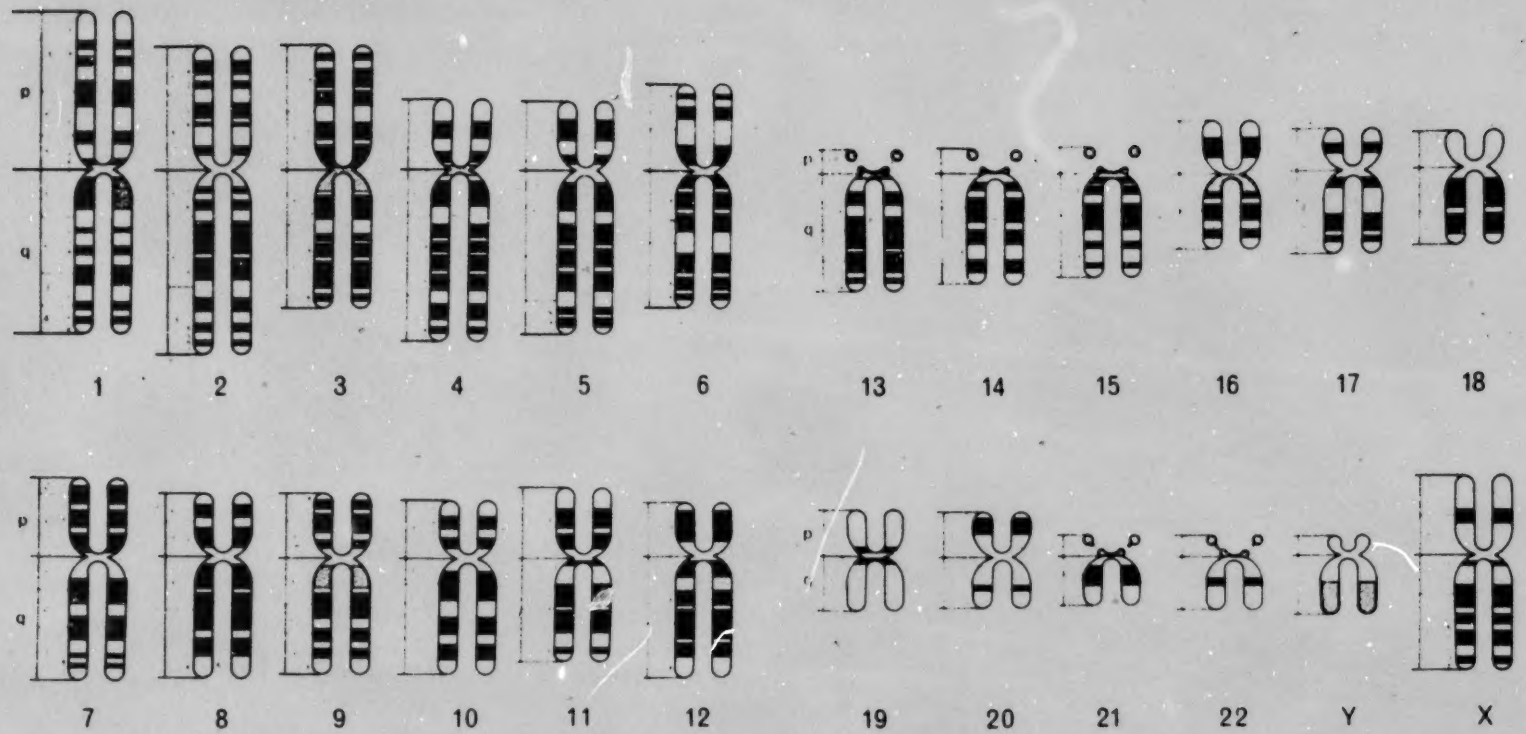
CHAPTER III

CHROMOSOME ERRORS

Quote: "It is still hard for me to understand how that little tiny bit there should make her the way she is. It is hard to grasp."

During the process of formation of the gametes and again in the process of fertilization there is room for error. THE TWO PRIMARY TYPES OF CHROMOSOMAL ERRORS ARE EITHER IN NUMBER OR IN STRUCTURE. WHEN THE RESULT IS TOO MUCH OR TOO LITTLE GENETIC MATERIAL WITHIN THE CELLS, A HANDICAPPED CHILD RESULTS.

Families should choose to read the subheadings in Chapter III that are most appropriate to them. Included is an ideogram of the chromosomes which may be used by the counselor. The geneticist should use the chart by marking in or out the segments of concern. This way all should be able to see precisely what chromosomal material is inexact in the child's bodily make up.



32

Negative or pale staining Q and G bands Positive R bands

Positive Q and G bands Negative R bands

Variable bands

Figure 8. IDEOGRAM Paris Conference (1971)

33

Numerical Abnormalities

It has only been since 1956 that procedures have been sophisticated enough to recognize that man normally has a total of 46 chromosomes. Errors in number were the easiest to identify with early laboratory equipment and techniques. The first error that cytogeneticists were able to determine in patients was the discovery in 1959 that persons with Down's Syndrome had 47 chromosomes in each cell instead of 46. Soon a few patients were determined to have 47 chromosomes in only some of their cells, a condition called mosaicism. In other situations some patients were found to have an extra piece of a chromosome, called a fragment, in all or some of their cells.

Nondisjunction

A cell with 47 chromosomes is referred to as a trisomy cell, tri meaning three; a cell with 45 chromosomes is referred to as a monosomy cell, mono meaning one. The most common cause of trisomy is an occurrence called nondisjunction, which occurs when chromosomes fail to separate, or to disjoin, properly and to go into separate cells at either the first or second stage of meiosis. This failure to separate results in one cell having two of one kind of chromosome and the other cell none. If the gamete with the extra chromosome unites with a normal gamete, the new individual will have 47 chromosomes with three of that particular one, instead of 46. The person will then be called trisomic for that particular chromosome.

NONDISJUNCTION AT MEIOSIS I

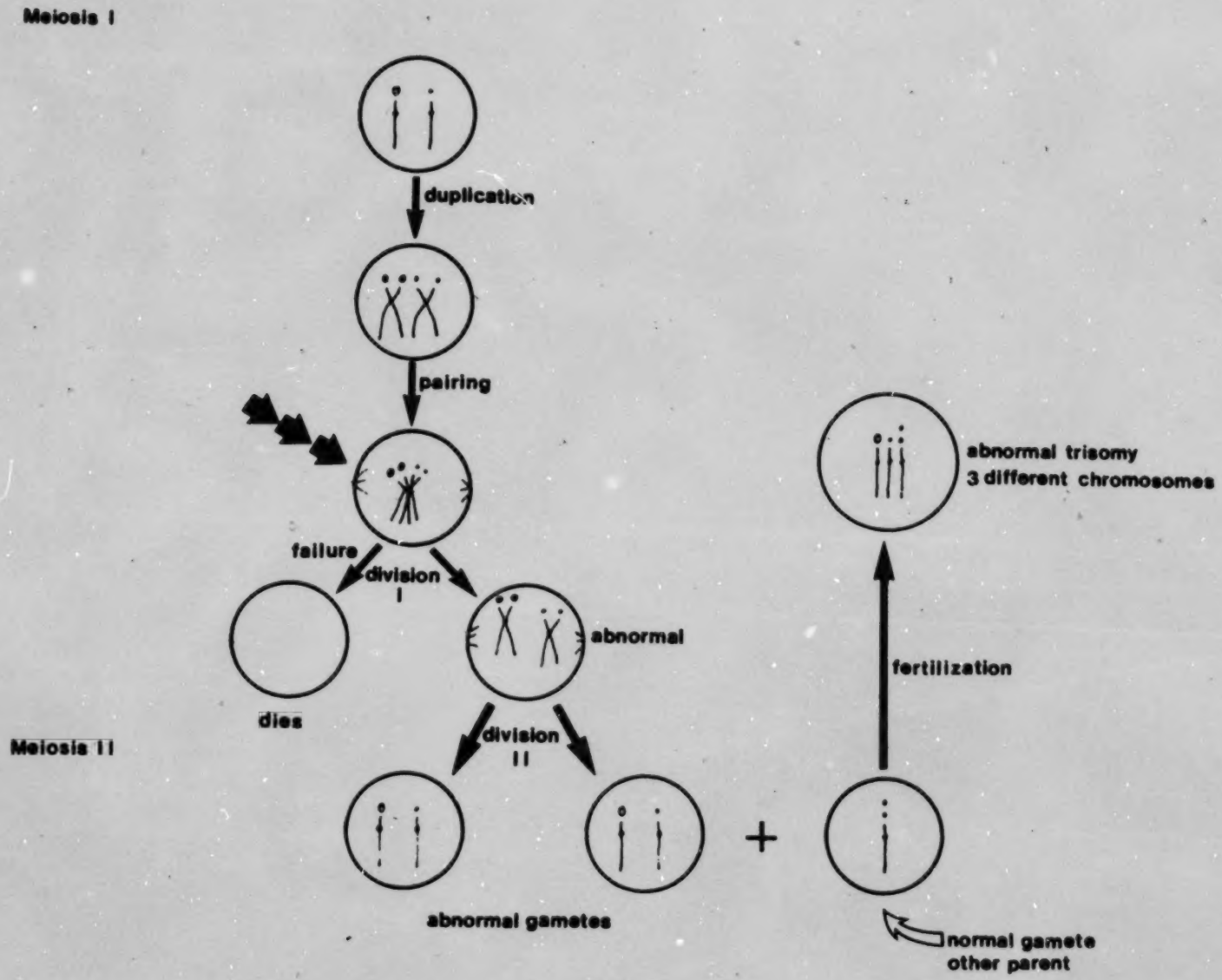


Figure 9. NONDISJUNCTION AT MEIOSIS I For simplicity, only two maternal and two paternal chromosomes are represented in this diagram. In normal meiosis I, after the cells divide, one pair of each of the chromosome pairs goes into a new cell, each called the daughter cell. In nondisjunction, this dividing process fails to take place and both chromosomes of a pair go into one cell and neither into the other. The cell missing a chromosome invariably dies. The cell with the two chromosomes may also die, but if it does not, it will enter into meiosis II. The two duplicated chromosomes split in half longitudinally at the centromere with each half randomly going to one of two new daughter cells, giving each new daughter cell an abnormal number of 24 chromosomes instead of the correct number of 23.

With fertilization by the normal gamete of the other parent, which has the correct complement of 23 chromosomes, the total chromosome count in the newly formed zygote is 47 instead of 46, creating a human with a trisomy condition.

NONDISJUNCTION AT MEIOSIS II

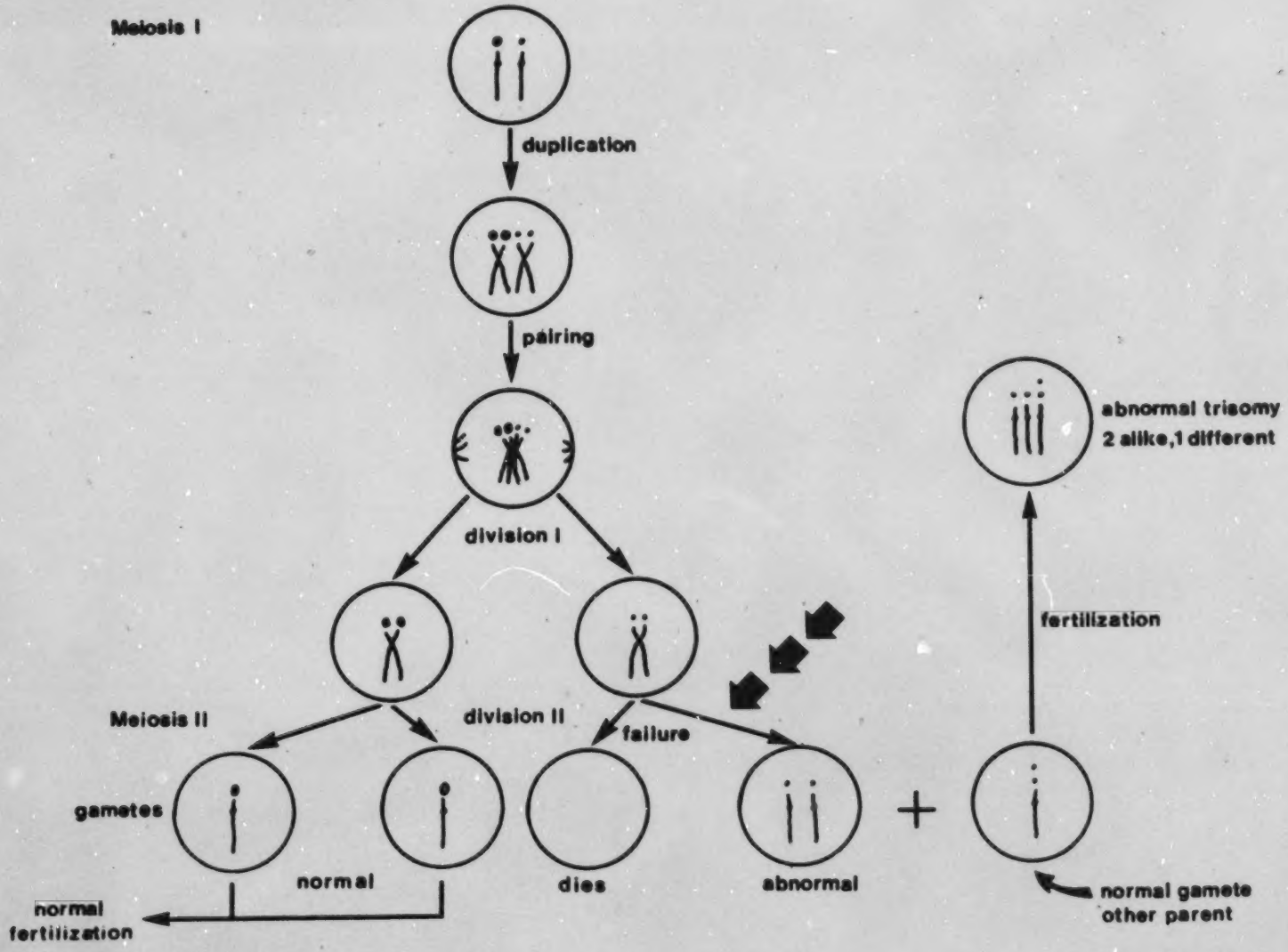
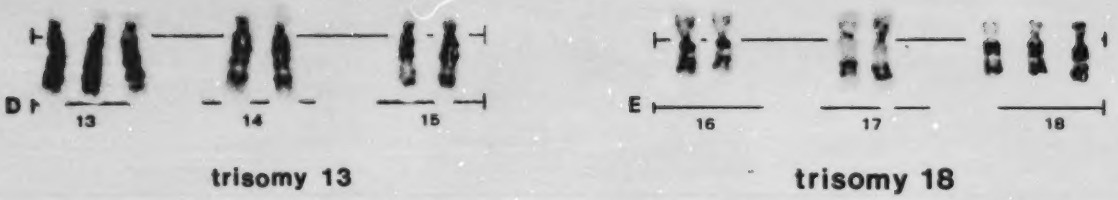


Figure 10. NONDISJUNCTION AT MEIOSIS II For simplicity, only two maternal and two paternal chromosomes are represented in this diagram. If nondisjunction occurs during meiosis II and pairing and meiosis I occur correctly, the duplicated chromosomes again randomly go to one of two new daughter cells. At this point, an error can occur in which one of the duplicated chromosomes does not split correctly. This results in two normal gametes, one gamete missing the chromosome and one gamete with the extra chromosome. If this last gamete is fertilized by the normal gamete of the other parent, the total chromosome count in the newly formed zygote is 47, instead of 46, creating a new human with a trisomy condition.

The most common chromosome error found in living individuals is the triplication of the entire chromosome number 21. Trisomy 21 or Down's Syndrome is one of the most common birth defects that is recognized in the newborn period. This means each cell in the body has 47 chromosomes instead of 46, the extra one being an extra number 21. While Down's is very common, it occurs by the same process that results in any other trisomy child. Children with Down's Syndrome have lifelong mental retardation. They also may have a shortened life span because of heart defects or immune problems, which makes them less resistent to infections, but they often do survive, probably because the 21st chromosome is the smallest and has the least amount of vital genetic material. Usually the larger the chromosomes involved, the more severe the clinical problems. This is why trisomy of the largest chromosomes is usually lethal and results in early miscarriages.

The other early identified trisomy syndromes occur with chromosomes 13 or 18. In both of these syndromes the children have multiple and severe malformations and usually do not live beyond infancy. However, there are children with abnormalities in these two chromosomes whose parents were told that their child's days, weeks or months were limited. Now, several years later, these parents are still struggling with planning for their severely handicapped, but still living child.

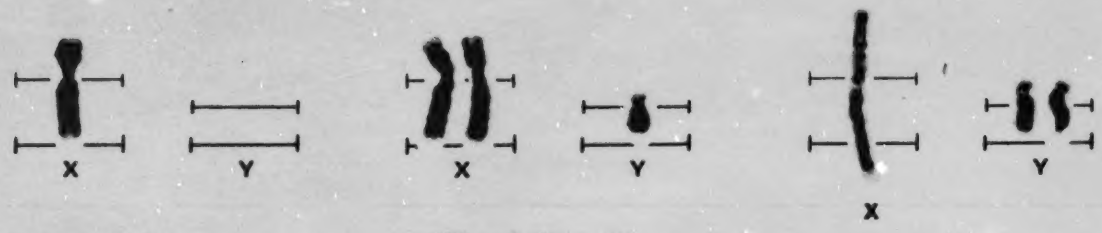


trisomy 13 trisomy 18

Figure 11. AUTOSOMAL CHROMOSOME SYNDROMES INVOLVING NONDISJUNCTION The rest of the chromosomes from these two separate individuals are normal. It is only chromosome number 13, or chromosome number 18, which is redundant, or trisomic.

There can be errors of nondisjunction in sex chromosomes also, the most common being a male with two X's instead of one, resulting in a 47, XXY, karyotype or in two Y's instead of one, resulting in a 47, XYY, karyotype. Males who have two X's are referred to as having Klinefelter's Syndrome. Characteristically, they are usually tall, sterile and may be mildly retarded.

If a normal gamete unites with a gamete that is monosomic then that resulting person will have only 45 chromosomes in each cell. There is only one monosomy condition that results in a human being capable of sustaining life. It is called Turner's Syndrome. Girls with this condition are missing a sex chromosome, resulting in a 45 XO karyotype. These girls are sterile and of short stature. They may have multiple health problems, including orthopedic, kidney, hearing and heart defects. However, Turner's Syndrome is the only major chromosomal abnormality so far identified that does not result in at least some degree of mental retardation.



Turners Sx. **Klinefelter Sx.**
45,XO **47,XXY** **XYY**

Figure 12. SEX CHROMOSOME SYNDROMES INVOLVING NONDISJUNCTION
The rest of the chromosomes from these three separate individuals are normal. It is only the sex chromosomes that are affected by being abnormal in number.

Mosaicism

Mosaicism is a mixture of two or more different cell populations. If nondisjunction occurs during mitosis in a single cell early in embryonic development, it will result in two cells with an abnormal number of chromosomes. When mosaicism occurs, one cell will have 47 chromosomes, the other will have 45 chromosomes. The cell with only 45 chromosomes usually dies so that the 47 count cell is left to proliferate, forming one cell line. However, the other cells that were present with the normal number of 46 chromosomes will also continue to divide normally, thereby resulting in a mosaic individual with two different cell lines.

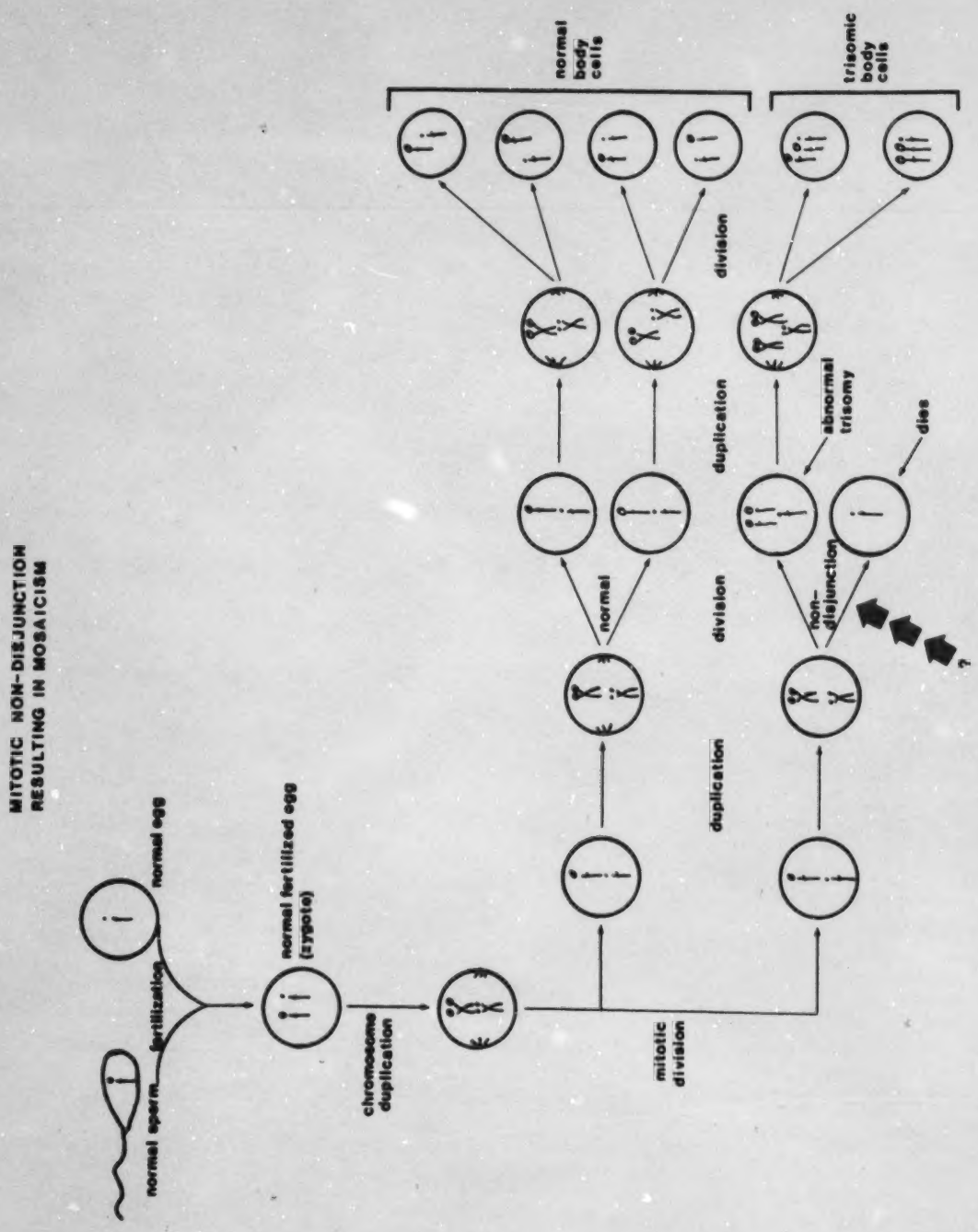


Figure 13. MITOTIC NONDISJUNCTION RESULTING IN MOSAICISM
Nondisjunction following fertilization, but occurring early in the embryonic development, results in at least two different cell populations. The percentage of abnormal cells depends upon the number of mitotic divisions that have taken place before the error occurs. In this illustration, the major cell line is represented by normal body cells containing 46 chromosomes. The minor, trisomic cell line, contains 47 chromosomes. Each cell line continues to proliferate independently of the other.

Less often there can be multiple cell lines creating complex mosaic combinations.

Fragments

Sometimes a karyotype will have what is referred to as a fragment, which is a small piece of chromosome material that is found in a range from a few to many cells. There are two types of such fragments, those that have a centromere called a centric fragment, and those without a centromere, called an acentric fragment.

As acentric fragments cannot divide, they are only found in occasional cells. If they are found in less than one out of every 20 cells studied, they are considered to be extra material of no significance.* In fact, most of us, if we examined enough cells of our body, would find some acentric fragments within these cells.

If a centric fragment is present in only one cell of a study of 20 cells, it is also ordinarily considered to be only an artifact and not representative of a true cell line.* However, when a centric fragment is present in most or all cells, it is significant. With new banding techniques, many of these fragments can now be identified as being a piece of a specific chromosome, thereby making the child a trisomy for that fragment of that chromosome.

*This does not hold true for the changes found in some leukemia cells and in some breakage chromosome syndromes.

9p trisomy

Figure 14. CENTRIC FRAGMENTS This partial karyotype contains a centric fragment of a submetacentric chromosome which has been identified as being the short arm of chromosome number 9, resulting in a patient with 9p trisomy syndrome. The rest of the long arm, which did not contain the centromere, has died off and disappeared.

Structural Defects

A person can be born with 46 chromosomes, but have something wrong with one of them. Such problems are called structural defects and come from a breakage and rearrangement of one or more of the chromosomes. It has only been since 1972 that equipment and procedures have been refined enough to allow complex structural rearrangements to be seen and analyzed, although prior to that time it was possible to identify that a piece of chromosome was missing.

The primary principle to remember in structural defects is that a break in a chromosome results in its having a raw edge. Raw edges seem to attract each other and subsequently try to attach themselves to each other; it is how they join that determines whether there will or will not be a structural defect and, if there is one, how severe a problem it will be. There are an almost infinite variety of errors that are possible within the chromosome itself which make each family's problem appear on the surface to be unique. As a matter of fact, breaks resulting in errors of some specific chromosomes are found more often than

one would expect if they were only random. When enough people are identified with having a similar error, a new syndrome is identified, such as the now commonly described 5p- or 18p- syndromes. Other errors appear to be single isolated incidents that so far have not repeated themselves. However, with new improved techniques, new defects will continue to be found that were formerly unseen.

Deletions

A chromosome that has a piece that has broken off it and then disappears is referred to as having a deletion. In fact, a small piece of chromosome without a centromere that breaks off usually does disappear unless it attaches itself to another chromosome which also has a raw edge.

It is usually possible to identify from which arm or which chromosome the piece is missing because that arm will be shorter than its mate. However, it is important to determine what piece may be missing for it may be a section from the end of the chromosome called a terminal deletion, or it may be a piece closer to the centromere not involving the end which is called an interstitial deletion. The clinical diagnosis depends on the identification of which of the numbered bands are actually missing.

5p-
terminal deletion

interstitial deletion
4p

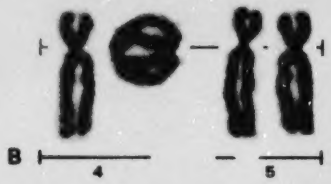
Figure 15. DELETIONS The left hand composite shows a partial deletion of the short arm on the right hand number 5 chromosome. This fairly common deletion syndrome is referred to as the Cri du Chat, Cat Cry or 5p- syndrome.

The right hand photograph shows an interstitial deletion involving the short arm of chromosome number 4. The missing segment is one of the larger dark areas; the terminal segment or end of the chromosome, which photographs as a fuzzy white band, is stuck back on intact to the end of the chromosome. This is referred to as an interstitial deletion of the short arm of chromosome number 4 and is not very common.

A fairly common deletion syndrome is the Cri du Chat or Cat Cry Syndrome in which the terminal end of the short arm of the number 5 chromosome is missing. This is technically referred to as 5p- Syndrome. Children with this condition are often recognized in the newborn period by their weak cat-like cry, due to an abnormality of the larynx. Such individuals are severely retarded and until recently were thought to have severely shortened life spans. However, many adults are now found in state institutions where they have been sheltered and protected for most of their lives. Thus, this severe abnormality is recognized as being compatible with adult life.

Ring

A ring chromosome is the result of another kind of deletion. Sometimes both ends will break off a chromosome leaving two raw ends. The raw ends then adhere to each other causing a ring. Depending upon the kind and amount of material lost, this can be a minor or a devastating catastrophe.



ring 4

Figure 16. RINGS Rings have been observed with almost every chromosome. The clinical picture of the patient varies depending upon the chromosome involved and the genetic material that is lost.

Isochromosomes

Sometimes a child will be born with 46 chromosomes, but one arm of one chromosome will be duplicated and the other arm will be missing. This is called an isochromosome. It is thought to occur when the chromosome splits horizontally instead of vertically. When this happens, it means that important material from either the top or bottom half of the chromosome is lost while material from the other end is duplicated, resulting in an individual who has only a single copy of one arm and three copies of the other arm within the pair of chromosomes.

46,XisoXq

Figure 17. ISOCHROMOSOMES These are most commonly found in the X chromosome, but may be found in an autosome. The principle of formation is the same in either case. The right hand X chromosome has a duplicated long arm thought to be caused by the chromosome splitting horizontally at the centromere instead of vertically. This results in an individual having three copies of the long arm, or q segment, and one copy of the short arm, or p segment.

Translocations

Translocations are chromosome rearrangements involving two or more different chromosomes. Translocations occur at the time of germ cell formation called gametegenesis (the process in which cells reduce from 46 count chromosome cells into 23 count chromosome cells). They can occur at either meiosis I or meiosis II and can be simple or highly complex. There are two ways that a translocation can present itself; it can be either 1) de novo or 2) familial. Each type can be balanced with no loss or gain of chromosomal material or conversely, each can be unbalanced with loss or gain of chromosomal material.

De Novo Translocations

A de novo translocation is the result of an isolated incident when both parents are found to be chromosomally normal. The cause of this accident during the gametegenesis is not yet clear although under investigation, but the result is either a

balanced or unbalanced translocation. The most commonly recognized de novo unbalanced translocation is identified in the small child through the investigation into the cause of the child's various handicaps.

A balanced de novo translocation results in a normal child and will probably not be detected, except by accident, in childhood. A PERSON CARRYING A BALANCED TRANSLOCATION IS COMPLETELY NORMAL IN APPEARANCE AND FUNCTION. A de novo translocation, however, has the potential to become a familial translocation because the child as an adult is itself at risk for having an abnormal child with a unbalanced chromosomal rearrangement. This is because translocations cause problems within the pairing process in meiosis I where an unbalanced gamete may occur and thus, when it is fertilized by a normal gamete, will result in a chromosomally abnormal child. This child will have either extra or missing material. The severity of the birth defect depends upon which chromosomes are involved and how much material is either missing or redundant.

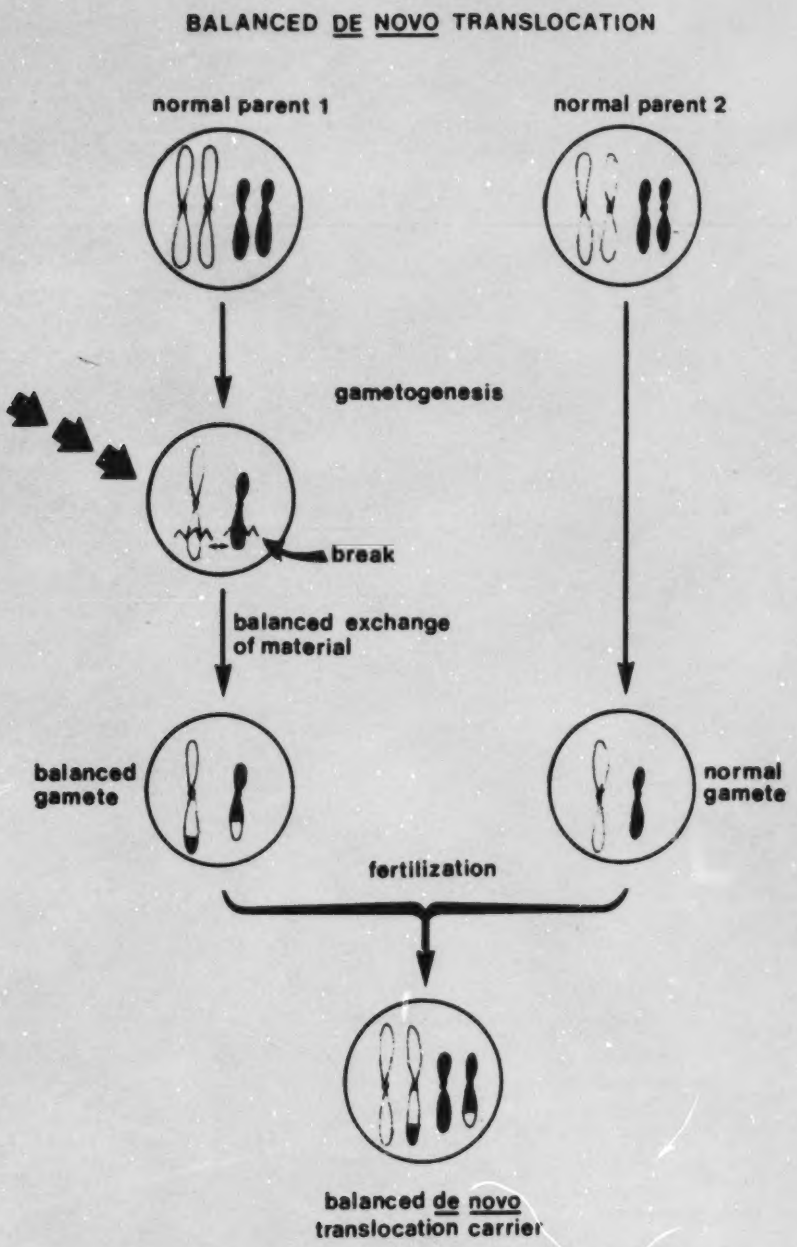


Figure 18. BALANCED DE NOVO TRANSLOCATION For simplicity, only two maternal and two paternal chromosomes are represented in this diagram. Both parents are chromosomally normal. A balanced de novo translocation occurs at some point during gametogenesis when there is an insult to the cell causing two chromosomes to break. The broken material from each chromosome adheres to the other, creating a balanced exchange of material.

If the two chromosomes, each with the other's material, travel together during random segregation, there will be no observable problem. Upon fertilization by a normal gamete, a clinically normal, but chromosomally abnormal human will result who carries a balanced de novo translocation.

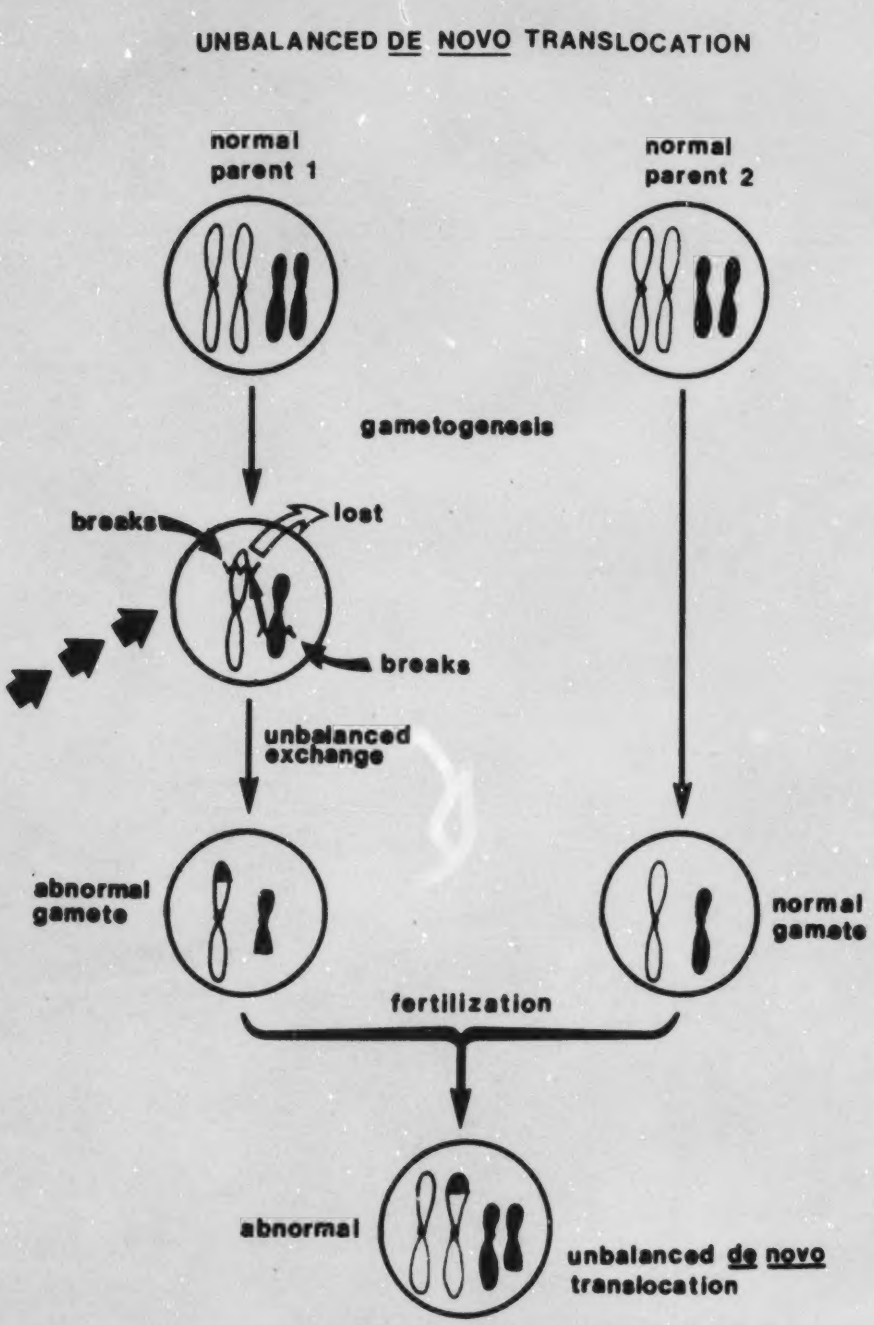


Figure 19. UNBALANCED DE NOVO TRANSLOCATION For simplicity, only two maternal and two paternal chromosomes are presented in this diagram. Both parents are chromosomally normal. An unbalanced de novo translocation occurs at some point during gametogenesis due to an insult to the cell; two chromosomes break, but instead of both broken segments reattaching themselves, one to the other, one segment may attach itself to the other chromosome while the other segment drops off and is lost. Fertilization of the abnormal gamete, with the piece missing, results in an abnormal child who carries an unbalanced de novo translocation.

Familial Translocations

A familial translocation is one that has been detected in more than one family member and has been demonstrated by direct clinical study, or by inference, to be inherited. For example, two siblings may be studied and found to carry the same translocation. If it is not possible to examine either parent, it can be inferred that one of the parents carries the same translocation by the fact that these rearrangements are so rare, for two sibs to demonstrate the same rearrangement without having inherited it from a parent is most unlikely.

A familial translocation may or may not result in a defective child. Again, as with a de novo rearrangement, it depends upon whether the chromosome abnormality is balanced or unbalanced. The most commonly recognized unbalanced familial translocations are also usually identified in the small child through an investigation into the cause of the child's various handicaps. A person who is a balanced carrier is said to be chromosomally abnormal. The person has all of the necessary material, but it is rearranged. A PERSON CARRYING A BALANCED TRANSLOCATION IS COMPLETELY NORMAL IN APPEARANCE AND FUNCTION. It is in the formation of the person's gametes where the problems may occur.

FAMILIAL TRANSLOCATION

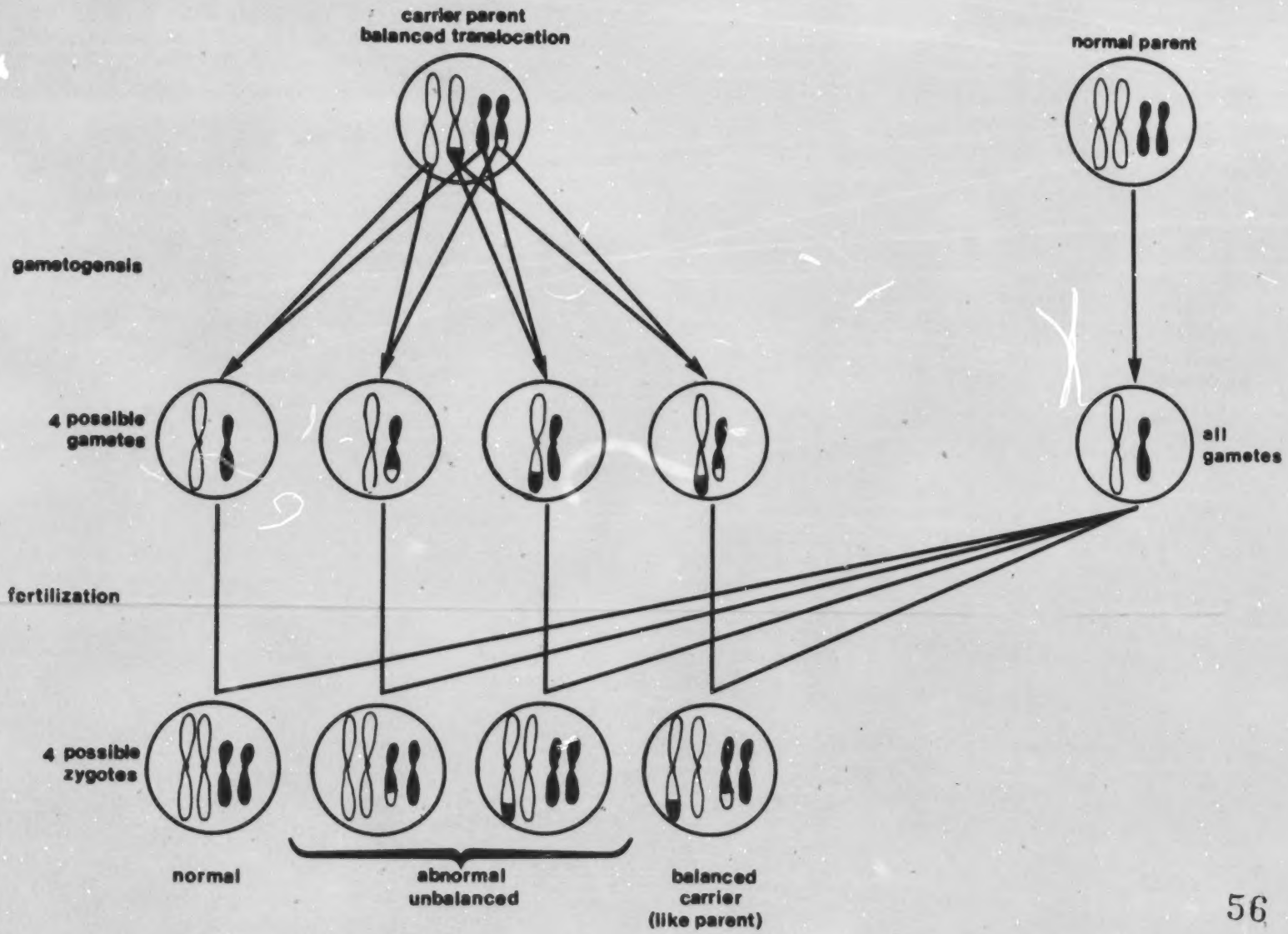


Figure 20. FAMILIAL TRANSLOCATIONS In this illustration, for the sake of clarity, the two pairs of chromosomes are referred to as the white chromosomes and the black chromosomes. A balanced carrier parent can produce four different gametes:

1. There can be a normal gamete which contains one entire white chromosome and one entire black chromosome.

2. There can be an abnormal gamete with one normal white chromosome and one abnormal black chromosome. The black is missing a piece of its material and attached in its place is an extra piece of white material. The chromosome is therefore trisomy for extra white material and monosomy for a segment of black material.

3. There can be an abnormal gamete with one normal black chromosome and one abnormal white chromosome. The white is missing a piece of its material and attached in its place is an extra piece of black material. The chromosome is therefore trisomy for extra black material and monosomy for a segment of white material.

4. There can be an abnormal, but balanced condition with both the abnormal white chromosome and abnormal black chromosome in the gamete.

Upon fertilization by the gametes from the normal parent, four possible zygotes can result:

1. The zygote can be normal, having the normal gametes from both the translocation carrier parent and the normal parent present.

2. The zygote can be abnormal, by having the abnormal chromosome with its missing section of black chromosome and its extra section of white chromosome fertilized by the normal parent.

3. The zygote can be abnormal, by having the abnormal white chromosome with its missing section of white chromosome and its extra section of black chromosome fertilized by the normal parent.

4. The zygote can be balanced like the balanced translocation carrier parent, having both the abnormal black chromosome and abnormal white chromosome present. Also, like the parent, this person will potentially make abnormal gametes.

JUST BECAUSE A PERSON CARRIES A BALANCED TRANSLOCATION DOES NOT MEAN THAT ALL OF THE GAMETES WILL BE ABNORMAL. In theory, for each person who carries a balanced translocation, fifty percent of the couple's conceptions should result in fetuses that are normal and fifty percent in fetuses that are abnormal. In actuality, this is fortunately not the case. In the well studied population of Down's translocation families, it is known that if the father carries a 14/21 translocation the chance of having an affected child is about 2-5 percent while the risk of a Down's child if the mother carries the translocation is about 10-15 percent.

There is insufficient datum to give an empiric risk figure for subsequent pregnancies to families who carry a rare balanced translocation, but it is known that the risk is low, substantially less than fifty percent.

Inversions

An inversion results when two breaks occur simultaneously in the same chromosome and a segment turns upside down before being reinserted and repaired. An inversion that does not involve the centromere is called a paracentric inversion. An inversion involving the centromere is a pericentric inversion. An inversion can also be de novo or familial. A PERSON CARRYING AN INVERSION IS NORMAL BECAUSE ALL OF THE GENETIC INFORMATION IS THERE; IT IS JUST REARRANGED. The danger lies in the formation of the gametes.

During meiosis when the maternal and paternal chromosomes in the carrier parent try to line up, the chromosome with the

9;12 FAMILIAL TRANSLOCATION

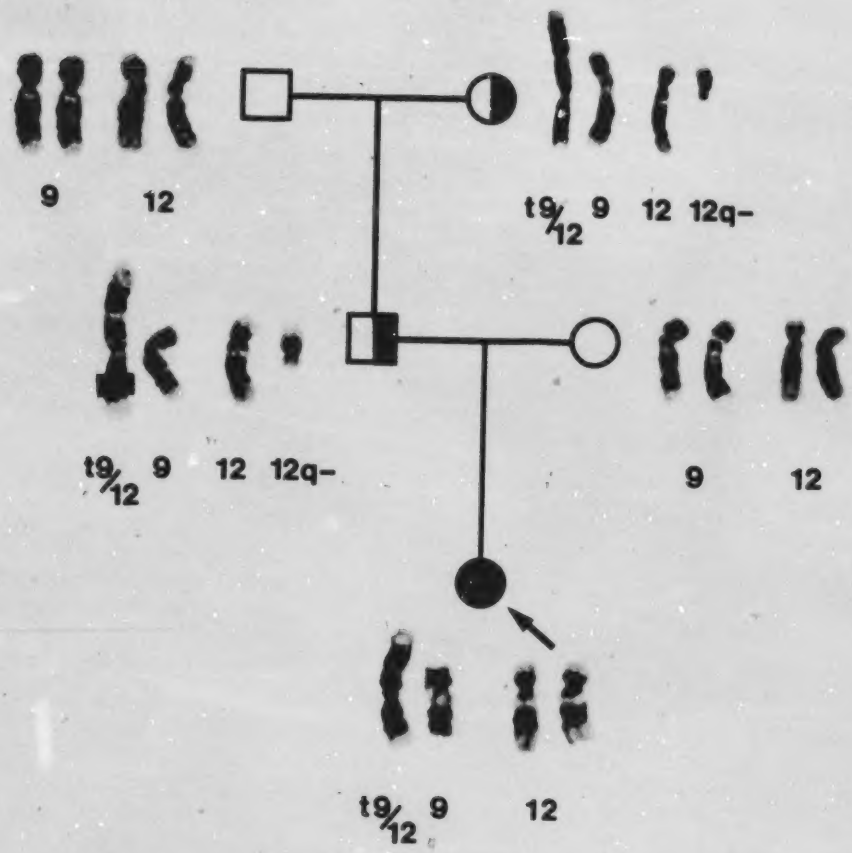


Figure 21. 9/12 FAMILIAL TRANSLOCATION This is a three generation karyotype/pedigree illustrating the inheritance of a two generation balanced translocation resulting in a chromosomally unbalanced offspring in the third generation. In the carrier, the long arm of the number 12 chromosome has been attached to the short arm of the number 9 chromosome resulting in a chromosomally balanced person. In the patient, however, the individual ends up with the normal number 12 chromosome, one normal 9 chromosome and one abnormal 9/12 translocation chromosome. The abnormal chromosome has extra 12q material attached to the short arm of the number 9 chromosome, resulting in its having three copies of 12q. This condition is referred to as 12q trisomy.

inversion has to form a loop in order to pair with the normal chromosome. If there is a crossover within the inversion loop, a normal chromosome, an inverted but balanced chromosome and two abnormal chromosomes will be formed. These abnormal chromosomes will have both duplicated (extra) and deleted (missing) chromosome material. If no crossover occurs, two normal chromosomes and two chromosomes with the balanced inversion will be formed. Each of these chromosomes goes into a different daughter cell. JUST BECAUSE A PERSON CARRIES AN INVERSION DOES NOT MEAN THAT ALL OF THE GAMETES WILL BE ABNORMAL.

Figure 22. PERICENTRIC INVERSION AT MEIOSIS Since the chromosomes pair much like a zipper, the inversion must form a loop in order to pair with the normal chromosome. If there is a crossover within the inversion loop, there are four possible gametes that may result.

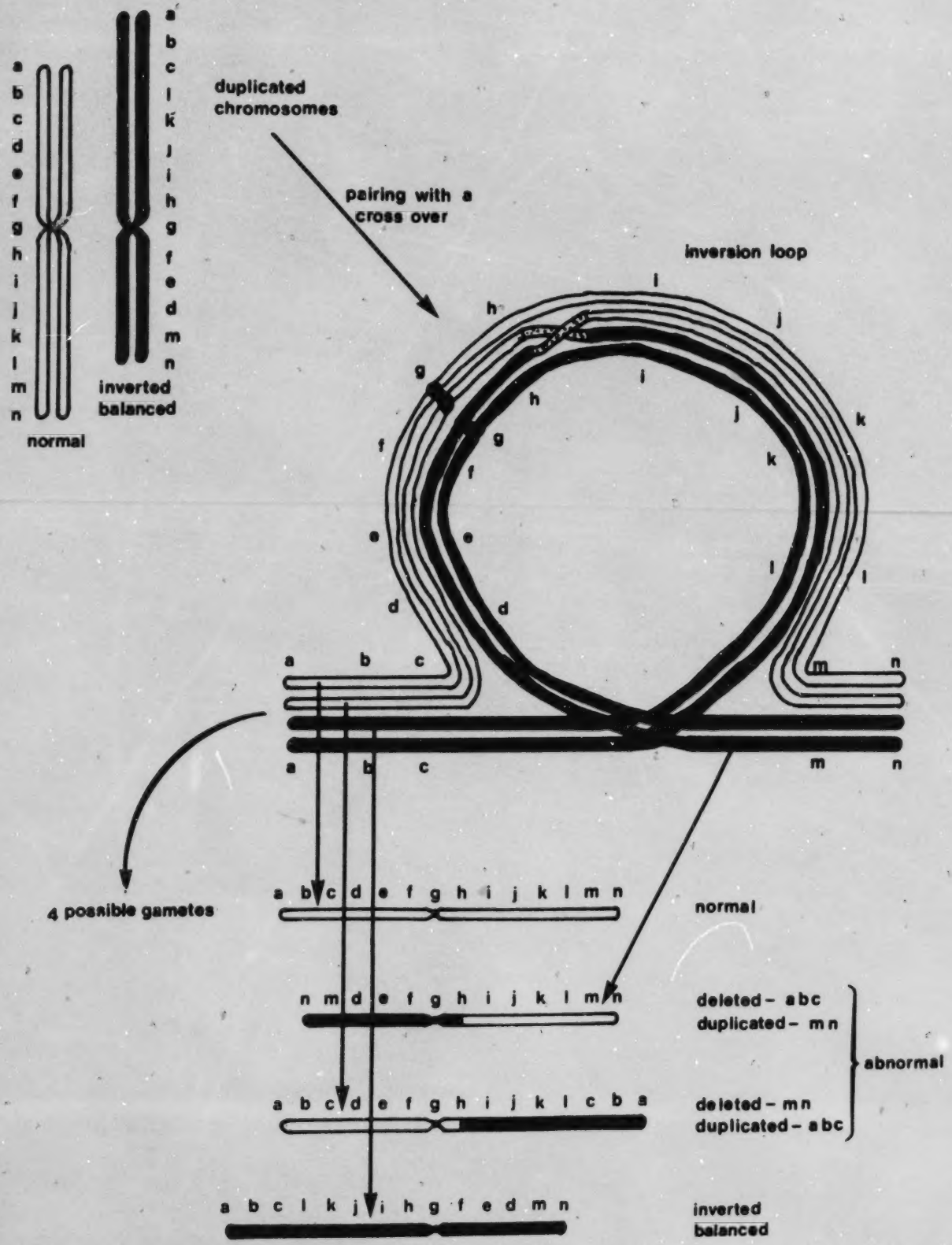
1. The gamete may be normal as in the first possibility where there is no rearrangement.

2. The gamete may have material missing from the short arm and extra material from the long arm added to the end of the short arm. This is called a short arm deficiency, long arm duplication condition and is shown in the second gamete possibility where the "abc" is deficient and the "mn" is duplicated.

3. The gamete may have material missing from the long arm and extra from the short arm added to the end of the long arm. This is called a long arm deficiency, short arm duplication condition and is shown in the third gamete possibility where the "mn" is deleted and the "abc" is duplicated.

4. The gamete may be a balanced inversion with all material present, but in an abnormal arrangement. This inverted chromosome is identical to that of the parent.

PERICENTRIC INVERSION AT MEIOSIS


a b c d e f g h i j k l m n
normal
a b c l k j i h g f e d m n
inverted balanced
duplicated chromosomes
pairing with a cross over
inversion loop
4 possible gametes
a b c d e f g h i j k l m n
normal
n m d e f g h i j k l m n
deleted – abc
duplicated – mn
abnormal
a b c d e f g h i j k l c b a
deleted – mn
duplicated – abc
a b c l k j i h g f e d m n
inverted
balanced

CHAPTER IV

COMMON QUESTIONS REGARDING THE DIAGNOSTIC EVALUATION

Quote: "For awhile I wished she had Down's or something because there are so many kids with Down's that at least you know what to expect, but then I thought in a way it was a way out for me because even though they can't offer a lot of encouragement, they don't have enough data to say a lot of bad things either. It has given me a little hope."

Most chromosome abnormalities are suspected during childhood* and to confirm the diagnosis, the child and parents may be sent to a genetics center for evaluation and counseling. This evaluation includes many dimensions. A family who is already anxious about their child may not appreciate the intimate probing into the family life or the careful scrutiny given to the baby who has already been labeled as different. Answering some of the most frequently asked questions about the scope and purpose of the diagnostic evaluation should remove some of the anxiety of the unknown.

What Should We Expect During the Clinic Visit?

A clinical diagnosis is that determination of the nature of the disorder which can be made with the eye and some basic examining room equipment. A clinical diagnosis is arrived at by two basic steps, by observing the patient and by searching medical literature for descriptions of children with similar symptoms. A cytogenetics diagnosis is accomplished in a laboratory

*This does not take into account abnormalities found through general population studies or through institution population studies.

using elaborate and expensive equipment and it confirms or denies the clinical diagnosis. For example, while Down's Syndrome was clinically recognized as a specific condition and described in the literature by Langdon Down in 1866, it was not cytologically confirmed until 1959. Trisomy 13 was originally described in 1657, but was not diagnosed cytologically until 1960.

There are several specific steps involved in a clinical diagnosis before a blood sample is sent to the lab. They include taking the family pedigree, obtaining a pregnancy and health history, obtaining a developmental assessment and performing a careful physical examination which includes an examination of dysmorphic features and a look at the dermatoglyphics or skin patterns on the hands and feet.

The Pedigree

A family history is the first step in a clinical evaluation. There are two terms often used interchangeably, but incorrectly in constructing a family history, family tree and pedigree. A family tree has a geneological focus and is used by many religious and social groups while a pedigree has a genetic focus with information collected in the hope that it will provide clues as to the genetic, or nongenetic, nature of the diagnosis in question. A pedigree is more than a mere diagram of family relationships; it is a genetic and general medical history of a family covering at least three generations.

Information is requested concerning any relationship between parents, such as a cousin marriage, or a known common ancestor. A counselor will ask about any apparent familial diseases, the causes and ages of death of deceased close relatives, as well as take a careful family history of spontaneous abortions (miscarriages)

or still births on either side of the family. This information is used to help determine if there may be a previously undiagnosed child with a similar problem in the family.

Most geneticists feel that in families in which there is a familial translocation, all adult members should be informed of the situation. It is up to the individuals at risk to decide whether they wish to have a karyotype done of themselves and their at-risk children to see if any are balanced carriers, but in order to do this they should be given the necessary information to make a meaningful decision.

It is quite natural that grandparents and aunts and uncles may be reticent to discuss painful memories as they may have unresolved feelings about children who failed to thrive, who died early on, or who were placed in institutions. However, when they realize that information about some of their children may be of help to their other children and their grandchildren, they may be willing to share as much information as they can remember.*

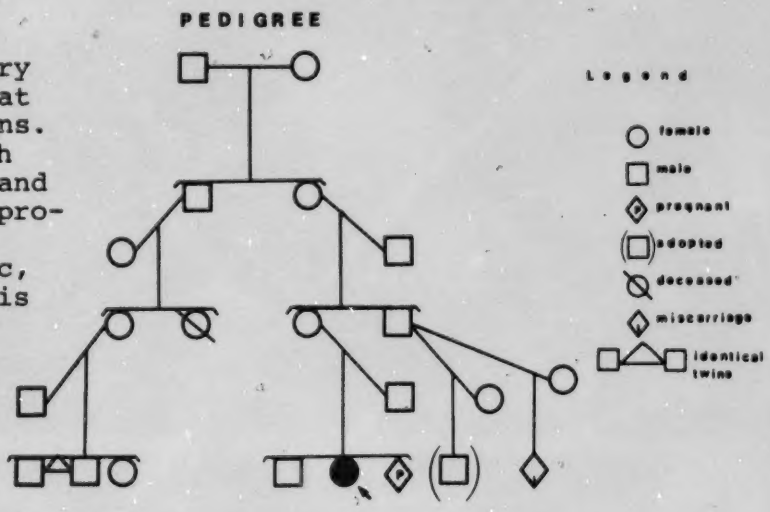


Figure 23. FAMILY PEDIGREE. The pedigree is a genetic and general medical history of a family covering at least three generations. All significant health history is recorded, and this data is used to provide clues as to the genetic, or nongenetic, nature of the diagnosis in question.

*See paragraph "Under What Circumstances Should the Rest of the Family Be Studied?"

Pregnancy History

A pregnancy history includes information about any illness or medications taken by the mother. It includes information about the onset and vigor of early uterine activity, the length of gestation (40 weeks is the average gestation time for humans), the type of delivery, the size of the baby at birth and any problems noted during pregnancy, delivery or newborn period. If this is not the first child, a comparison is made of this baby with prior siblings. If this pregnancy was different, the question is asked, "How did it differ?"

The answers may determine at what point in gestation the problem arose and may distinguish between an early embryonic error and a later environmental insult, such as an intrauterine infection.

Developmental History

How has the child continued to grow and develop since birth? What, if any, have been the health problems? What have been the developmental milestones? (The age when the baby sat up, crawled, stood up.) Are they delayed and, if so, how seriously? A developmental assessment by a professional trained in child development or, depending upon the age of the child, psychometric or intelligence testing by a psychologist may be requested. These tests not only determine the level of the child's functioning at the time of the evaluation, but they also establish baseline data for serial measurements. By measuring a child several times over a period of years, the rate of growth and development can thus be charted.

There are two purposes for these tests. Autosomal chromosome abnormalities invariably mean some degree of intellectual delay,

ranging from mild to severe, depending upon the exact chromosome material involved. For well established conditions, these tests can help provide confirmation of the diagnosis and parents can be counseled according to the established data. Or, in the less established abnormalities, where there is little or no datum regarding intellectual development and ultimate educational potential, these tests are a tool for collecting new data. In newly determined chromosome errors, serial testing will establish information as to specific patterns of development, thereby obtaining new data for subsequent families who encounter these problems so that accurate information as to intellectual development can be given early.

Physical Examination

By the time an embryo is 2 months old, often before the mother is sure that she is pregnant, most of the child's body systems such as the central nervous, skeletal, heart, lungs, digestive, urinary, and genital have been formed. Because the chromosome error has existed since the time of conception, many of these systems will be affected.

In evaluating a child, the specific routine starts by the interviewer making general observations. Is the child large or small for his/her age? Is the head size macrocephalic, too large, or microcephalic, too small? Does the baby have a peculiar cry? What is the baby's general overall appearance? The answers to these questions result in a general gestalt or impression. The subsequent exam is a refinement of the original impression.

Along with mental retardation, the other most consistent finding in a child with a chromosome abnormality is some degree

of size abnormality, usually growth retardation, which again can range from mild to severe. Rarely, as in 12p trisomy are children excessively heavy.[6] Therefore, careful measurements of length and weight and head circumference are made and recorded to establish current size and to establish growth rate patterns.

After establishing the baby's body and head size, the features of the baby are observed, starting at the top of the head and working downward, asking, "What is the size and shape of the face, forehead and ears? Are the eyes wide spaced or close together? Are they large or small?"

One thing a physician must do is to sort out what belongs to the family and what is possibly abnormal. A distinctive nose might belong to granddad, or an ear's shape might be just like mom's. Hypertelorism, widely spaced eyes, is considered to be quite attractive and it is necessary to distinguish that which is a fortunate cosmetic feature inherited by both big sister and baby from that which might be a diagnostic clue. Most facial feature sizes, shapes and locations for the general Caucasian population are charted on graphs in genetics textbooks. Therefore the doctor may take measurements of both the baby's and other family members' features to see if the features fall within the normal range of the rest of the population, within the normal range for the family or if they are significantly different, making the baby dysmorphic.

Dermatoglyphics, "derma" meaning skin, and "glyphics" meaning channel or groove, is the study of the fine ridged patterns on the fingers, palms, soles of the feet and toes. They are studied because there are distinct dermatoglyphic patterns for some cytogenetic syndromes. Skin ridge patterns are fully developed before

birth and never change during life. Although there is little known concerning the developmental mechanism that determines ultimate ridge patterns, it is known that they develop in very early fetal life and that they are in part genetically determined. Cytogeneticists are currently collecting data and studying the correlation between individual chromosome aberrations and dermatoglyphic features. This, hopefully, will lead to further knowledge in the exploration of early embryonic development.

One advantage in using dermatoglyphics as an aid to diagnosis is that it is quick, inexpensive and painless. Dermatoglyphic patterns can usually be seen by the naked eye or in the case of small children who have very fine ridges, with the aid of a lighted magnifying glass. As basic patterns on the fingers, palms, soles and toes are all previously determined and labeled by prior population studies, the patient's prints are observed and recorded against this established data.

It is this collection of signs that forms a distinctive pattern which contributes to the tentative diagnosis of a specific syndrome that in turn leads to the request for a karyotype. Since there are several chromosome abnormalities which are already described in the literature as specific syndromes, often a clinical diagnosis of a child can be made by comparing the observations to the described syndrome. Cytogenetic studies then confirm or deny this clinical diagnosis.

For example, 5p-, Cri du Chat or Cat Cry Syndrome, frequently results in a weak cat-like cry caused by the abnormal larynx. This abnormality is well described and a baby is often originally identified in the newborn nursery. It has been known that children born with aniridia, (absence of the iris), have an

increased chance of developing a malignant tumor, called a Wilm's Tumor, of the kidney. It has only been recently discovered, however, that there is a chance that persons with these two handicaps plus developmental delay are missing a small segment of the short arm of chromosome 11, called 11p- Syndrome. Mosaic Trisomy 8 often includes as one of the findings persons with missing patella or kneecaps. While it is understood that the cause of these problems stems from the missing or redundant chromosomal material, the exact number of unbalanced genes involved is not known nor is the mechanism for triggering the variety of errors found in the eyes, kidney, voice or knees.

Small deletions and trisomy fragments in the largest chromosomes have recently been described in the literature; however, whole trisomies such as with the number 1 are not yet associated with any definite clinical syndrome. This is undoubtedly because any structural or numerical anomaly of these chromosomes is probably fatal in early embryonic development and errors in the largest chromosomes have so far only been found in very early spontaneous abortions.

When these basic facts are understood, it can be seen why pediatric geneticists often can diagnose a child as having a chromosome abnormality by a short period of observation and examination. They may be certain enough of their diagnosis that if the initial cytogenetics studies come back as normal, they may pursue the question with more complex lab procedures. This continuing effort may take years. As a consequence, many children who were suspected of being chromosomally abnormal some

years ago, but who were not confirmed as such by early lab work, are now with the advent of new techniques, being reevaluated with positive results, confirming earlier suspicions.

How Are Chromosomes Studied?

Once it has been determined that a karyotype is warranted for a definite diagnosis, a sample of blood of one to five cc's (five cc's equals one teaspoon) is taken, usually from the arm or in the case of a very small infant, from some other large, easily obtained vein. As the test itself takes several days to complete, it is a time of fear and anxiety for a family.

Basic Steps of Preparation

The principle steps in preparing a karyotype for analysis are similar, with minor variations from lab to lab. The steps are as follows:

1. The blood is put into a tube containing an anticoagulent, which keeps the blood from clotting, and is allowed to sit until it settles into three layers. The red cells sink to the bottom; the white cells, which contain the lymphocytes, the material to be studied, are in the middle; and the plasma rises to the top.
2. The white cells are removed from the tube, placed in a rich protein broth with a growth stimulant and incubated at body temperature for about 72 hours. In the broth the cells grow and divide rapidly, creating enough cells to observe.

3. When there is sufficient cell growth, a chemical is added to stop the cell growth at the state referred to as metaphase. (As mentioned previously, it is at this point the chromosomes are most easily distinguishable, being puffy and held together at the centromere prior to splitting.)
4. A solution is then added which causes the nuclei to swell and the chromosomes to separate from each other.
5. A fixative is added to preserve the cells.
6. This suspension is then dropped from several inches away onto the slide causing the cell to burst open and the chromosomes to spread so they may most easily be seen.

With the completion of this basic preparation, the cells are then ready for staining and for viewing under a camera equipped microscope. The stains and various treatments used depend upon which will best reveal the banding pattern desired.

Staining Techniques

As seen by the following examples, the same karyotype, depending on how it is stained, can give differing pictures. By being able to bring out different areas of the chromosome, more information is obtained. Benign differences can be recorded. Normal variation is one of the key elements in eventually identifying abnormal chromosomes.

Elongated Chromosomes

A new technique has brought about the ability to accumulate

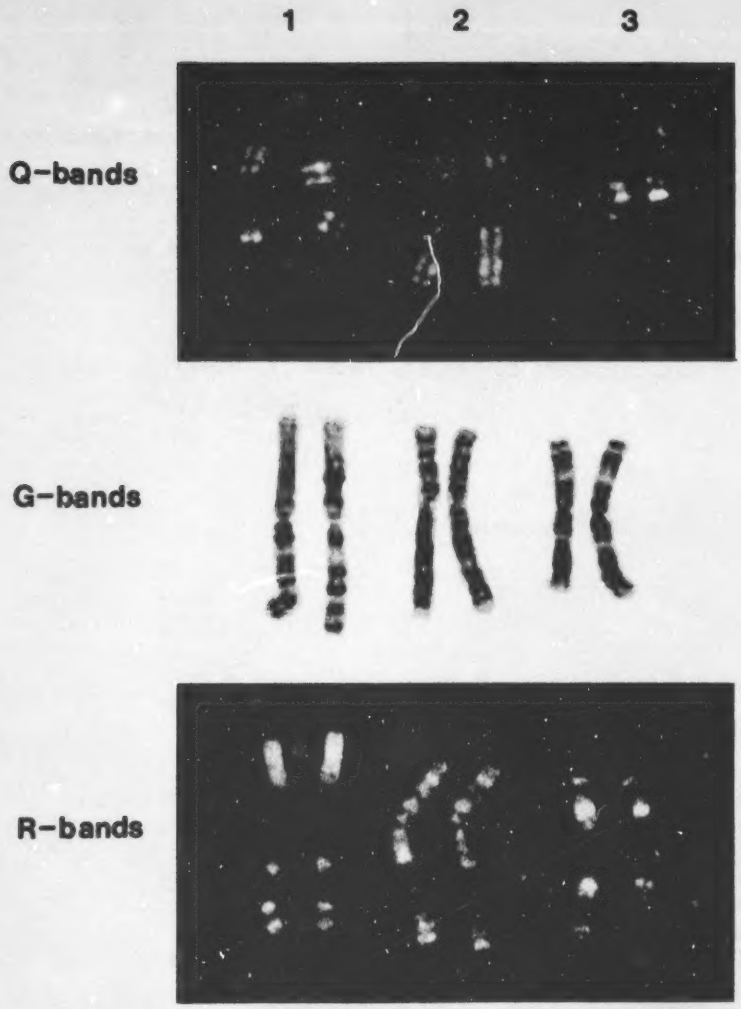


Figure 24. VARIOUS STAINING TECHNIQUES USING CHROMOSOME NUMBERS 1, 2 and 3 These chromosomes have been photographed after having been treated with three different stains. The various stains bring out different bands.

Q-bands (quinacrine) do not stain the ends, as shown in the number 1, very densely, but may stain the centromeres of the number 3's very brightly.

G-bands (Giemsa) basically stain the same regions as Q-bands, but generally more bands are visible with this stain as exemplified with the number 2 chromosome. Some variable regions as the number 3 centromeres do not stain with G banding.

R-bands (reverse) generally stain the opposite regions that are stained by the Q and the G-bands. As can be seen, the ends of the chromosomes, which are pale with Q and R-bands, stain very brightly with R banding.

chromosomes at an earlier stage in mitosis before they have had a chance to condense. At this step, the chromosome stretches out into a long strand so that more bands are visible. This chromosome can then be compared to new ideograms that are being designed to diagram these newly identified bands. As a result of this technique, extremely small deletions, inversions, or additions of material can be seen and, in many cases, ultimately identified.

Chromosome 2

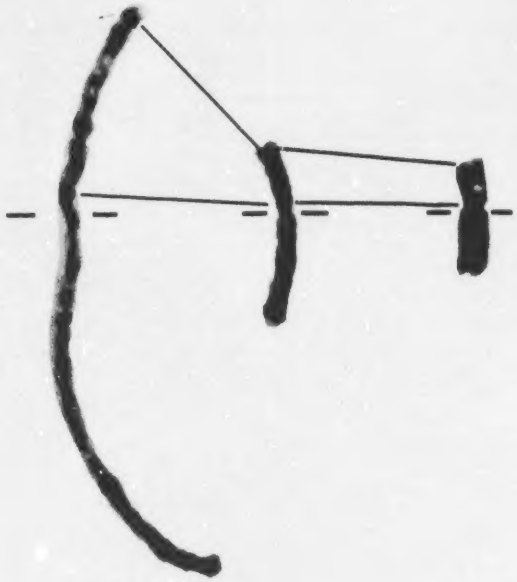


Figure 25. ELONGATED CHROMOSOMES Advanced laboratory techniques allow longer chromosomes to be studied. The same chromosome can be seen at three different lengths. The chromosome on the right is in a later stage, just before division, resulting in a more condensed chromosome. The one in the middle is seen during an earlier stage of metaphase and the one on the left is from very early metaphase. The longer the chromosome, the more bands are visible.

Because this technique is so new, a final numbering system has not yet been determined. This may be done at a conference soon. This numbering system will then become standard until even newer techniques reveal even greater variety in the chromosome bands, at which time it will too become obsolete and replaced with an even newer chart.

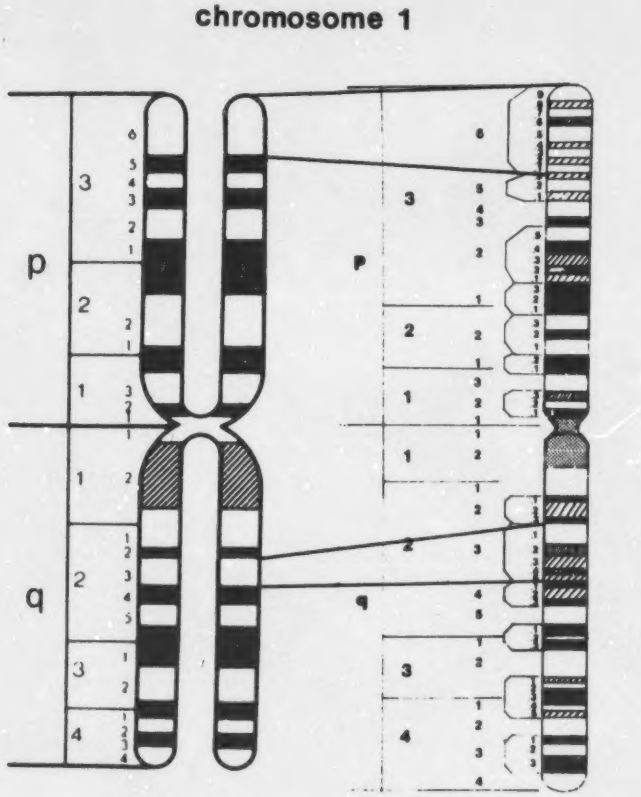


Figure 26. NEW IDEOGRAM SAMPLE The number 1 chromosome on the left is from the original Paris Conference ideogram of 1971. The one on the right is a more recent stylized version showing many more bands (Francke 1978). For example, p36 (pronounced p three six, not p thirty six) now has nine new subbands that can be clearly seen and q 2 3 has five newly identified bands.

Other Tissues Studied

While blood is the easiest material to obtain for cytologic studies; it is not always sufficient for more precise evaluations.

The second most common tissue examined is skin or fibroblast. A skin biopsy is a minor procedure, but one that is frequently distasteful to parents. However, most healthy children in the course of their activities will receive far more serious bumps and scrapes than the injury incurred by a skin biopsy and such injuries obtained accidentally are usually treated at home quite successfully with a kiss and a bandage. For children who already have multiple problems, however, a skin biopsy often seems like one more insult that must be endured.

Skin is used when it is necessary to consider another tissue of different embryologic origin than blood; it may show, in the case of suspected mosaicism, a second cell line. Fibroblast material is not used routinely for original studies, however, as it is much more difficult to grow and harvest and is more expensive to culture than is blood.

The procedure itself is extremely simple. A small area of the forearm is sterilized by a skin cleanser and an alcohol swab and the skin is anesthetized with the injection of a local anesthetic. A small nip of the skin or derma is removed either with a pair of sharp pointed scissors or with a special punch designed for the purpose. A sterile bandage is applied to the site and the patient is requested to treat it as he/she would any other minor wound.

The primary difference in culturing blood and in culturing skin is in the time involved; a skin biopsy takes three to four weeks to complete. It is in the primary steps that differences lie in the preparation of lymphocyte and fibroblast material.

1. The piece of skin is minced extremely fine and it is placed inside a plastic sterile flask.

2. A rich nutrient broth is added to feed the skin tissue. This broth is changed frequently to keep it fresh and the tissue healthy and growing.
3. The skin adheres to the flask and sends new cells spreading along the bottom of the flask.
4. After three to four weeks when sufficient cells have grown, the cells are carefully lifted out of the flask and then harvested in a process similar to blood studies.

Bone marrow is frequently used for obtaining a chromosome analysis when results must be obtained fast, such as at birth when surgery may be imminent. Results from a bone marrow chromosome evaluation can be available within 2-4 hours, if urgent.

Bone marrow looks like thick blood. It is obtained from the marrow or middle of the bone and is extracted from either the sternum (breast bone) or the iliac crest (top of the hip bone) in adults or from the tibia (shin bone) in children by a needle designed for the purpose. Bone marrow cells do not need stimulation; being a rapidly growing tissue, the cells can be harvested almost immediately.

Bone marrow is not used for routine exams as a bone marrow extraction is considered to be a minor surgical procedure. The results of this invasive and more expensive procedure are more often of poorer quality than are the results of studies of lymphocytes and skin cells.

Under What Circumstances Should the Rest of the Family Be Examined?

Clinically, there are three primary circumstances where a

physician may suspect a familial translocation and suggest further family studies:

1. If the couple has a child with an unbalanced translocation, both parents should be studied.
2. If a sibling or parent is found to have a balanced translocation, other at-risk members should be studied or,
3. If a couple has had three or more spontaneous abortions and other causes for this recurring problem have been ruled out, a balanced translocation in one partner may be considered.

When an unbalanced translocation is determined in the patient, the next diagnostic step is to examine each parent's chromosomes to confirm or deny the presence of a balanced chromosome translocation or mosaicism in one of them. THE CHANCE OF A PARENT CARRYING A BALANCED TRANSLOCATION IS NOT COMMON as there is less than a 50% chance that the condition will be familial. When the parents' chromosomes are normal, the child's condition is considered to be de novo.

It is when a parent is discovered to be a balanced carrier that extended family studies on that parent's family are warranted. The scope of the study varies from genetics center to genetics center, depending upon their particular philosophy concerning outreach studies, their funding sources, their research capability and certainly upon the family's interest. Minimally, however, the original family should be counseled regarding the possibilities of a balanced translocation running through their family, and the family members themselves should help the counselor construct

an accurate pedigree to determine those family members at-risk. The family should then contact their own family members with this information so that they may feel comfortable in calling the genetics center to request counseling for themselves.

When communication within a family is open, extended family studies can be accomplished with a minimum of distress and family members may develop a sense of empathy and support among themselves as they approach this new problem together. Sometimes, however, poor communication, prior family frictions, or lack of understanding of the meaning of the diagnosis may create new anxieties and fears and produce anger and hostility among the various members. When this situation arises, there are several problems of right and wrong for both the families and the genetics center to consider, such as problems surrounding confidentiality and individual rights of the initial family versus the possible consequences of anguish and suffering another family segment may endure from having the knowledge of the situation kept from them and an abnormal child be born. How this problem and its various consequences is handled involves a basic philosophical approach that each center must resolve according to its previously determined code. Ethical questions arising from the use of genetic knowledge are ones that are discussed frequently during genetic conferences, and during special sessions designed for the discussion of moral issues.

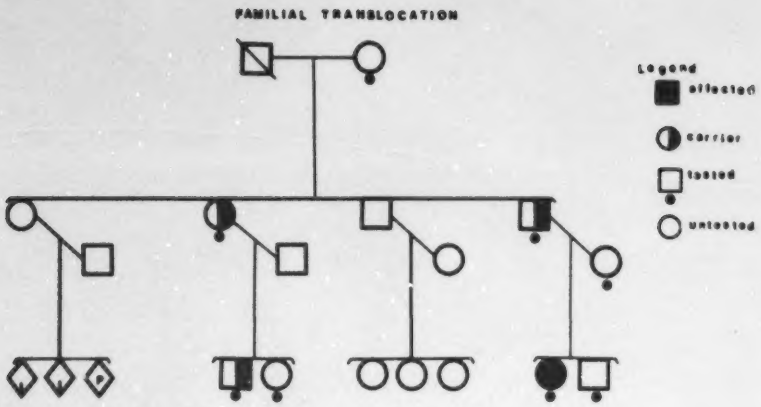


Figure 27. PEDIGREE OF A FAMILIAL TRANSLOCATION This pedigree of a family at risk for carrying a chromosome translocation indicates which family members have been studied, which members are unbalanced and affected, which members are clearly at risk as being balanced translocation carriers and which family members have not been studied.

The purpose of this type of pedigree is to show at a glance not only the family composition, but the extent of the potential problem.

CHAPTER V

RESEARCH

Quote: "What do you do when you ask the doctor what to expect and he says we don't have a hundred cases to go by, you are the book. How long can you go on being completely alone?"

Except for the splitting of the atom there has been no other occurrence in the twentieth century that has changed the outlook and expectation of man as has the beginning of understanding the structure, the composition and the internal chemistry of genetic matter. Because basic research in genetics has only been advanced since the 1930's, many persons erroneously feel that the field of heredity and inheritance is new. In reality it has been recognized for many years that cells are the basic structural unit of all animal and plant tissue. In 1865 man was able to add special dyes to cells and see under simple microscopes the thin long strands of chromatin. Nevertheless, although they had been observed for some time, it was not until 1900 that these strands, called chromosomes (chroma, a Greek word meaning color, and soma, a Greek word meaning body) were suspected of being carriers of inheritance.

In 1923 it was estimated that man had 48 chromosomes. It was only in 1956 that modern technology gave us the correct count of 46; new information is being published on a daily basis. This knowledge has occurred during the lifetime of most persons who are now in their child bearing years!

How does a geneticist arrive at an accurate diagnosis,

probable prognosis and valid recurrence risk for a family when the precise chromosome error under question is rare, and the precise variation in the exact amount of material involved is possibly unique to that family? The continuing quest for answers must cross the line between diagnostic evaluation and research, for it is only in the constant accumulation and tabulation of new data that answers to recurring questions can be obtained.

An orderly and ethical system has been designed to handle the awesome responsibility of this new and valuable information. Confidentiality versus common good is the ethical issue that remains at the core of all serious clinical research. Individual confidentiality is respected by using clinically unidentified case studies of persons who have given their permission to be described in the literature. Group data are collected by the accumulation of statistical evidence with little identifying reference as to the individual source. Nevertheless, it takes constant sensitivity and surveillance to supervise families' needs for confidentiality, while at the same time eliciting the necessary cooperation in order to gather information for the further expansion of genetic knowledge.

To complicate the delicate question of medical research further, the media occasionally stresses the sensational, the bizarre and the profane. Even when such stories are accurate, the exciting part of the story may be taken out of context. Thus, when presented to a public whose backgrounds in science may be sketchy, it may do more to alarm and confuse than to enlighten and assure. As exciting as the concepts of some basic research are, the goal

of this chapter is to give information that may be of practical application to a family in the reasonable future, thereby affecting a productive understanding of the requests made to a family by a research team. By having this basic understanding, a family can reach an educated decision regarding its agreement for participation in a project or ongoing study.

Clinical Research

The preponderance of research today in the field of chromosome abnormalities is primarily clinical, thereby providing for the gathering of data regarding specific chromosome errors and further identification of these errors.

With the focus of clinical research lying in syndrome identification, the goal should ultimately allow the geneticist to examine a patient, to analyze the chromosomes and to be able to determine what specific genetic material is extra or missing; then, based upon the knowledge of other similar patients, to be able to answer parents' most burning questions involving cause, anticipated health and developmental problems, probable intellectual functioning, approximate longevity and the risk for recurrence.

In order to reach this goal there are two primary tasks to be completed: 1) to observe children with known chromosome abnormalities over several years of development and, 2) to identify exactly what genetic material is extra or missing. Since the field of cytogenetics is still new and information sparse, it will take several years before these answers can be forthcoming for any one chromosome abnormality. While questions will always have to be answered in the same general terms as those given to any parent

who wonders what his children's general health, educational level, success in life and ultimate longevity will be, only by data collected by observing many children through many years will families with children with specific chromosome abnormalities eventually be given generalized ranges of predictability.

It is with this goal in mind that children are evaluated throughout their years, while their general health is monitored, their development is assessed and the extent and breadth of their various handicaps is tabulated. It should be mentioned that with the advent of new educational opportunities for the handicapped and the thrust towards normalization this procedure has become more complex. A child left passively in an institution does not exhibit the same advances as does a child reared in a family atmosphere within the community and public school system. Therefore, standards of development are being revised upward for even the multihandicapped child.

Data from these longitudinal evaluations are compiled by communication with other centers through collaborative studies and, eventually, compiled by computerized data. The primary purpose of this joint undertaking is the pooling of knowledge. It is only through the combining of individual efforts that sufficient data can be obtained to provide answers regarding diagnosis, prognosis and recurrence.

Collaborative studies are joint studies done in cooperation with other centers. Because of the large number of total chromosome abnormalities, but the small number of specific errors, the only way to obtain sufficient data to establish reliable facts

and figures is through several centers pooling their studies. These studies may be the result of loose informal agreements or the result of specifically funded and contracted research grants. Information concerning mutual areas of interest is also derived from personal communication, national and international meetings and reading current literature.

Several centers are currently working on perfecting an efficient and meaningful system of storage of cytogenetic and clinical data. A general repository should eventually be of value to any physician requesting information about the incidence or a specific chromosome abnormality, including its general and specific features and the manifestation of its abnormalities.

Cytogenetic Research

The second task, identifying what genetic material is extra or missing and the source of the error in any one affected individual, is accomplished in the cytogenetics laboratory.

Many inherited traits are polygenic, meaning there is more than one gene for more than one trait. It is known that all chromosome disorders involve multiple genes. Any error large enough to be observed must involve many genes; that is why so many systems within the body are affected. The primary thrust of most cytogenetic research lies in identifying the location of genes within the chromosomes.

There are many ways of testing for many gene products, but as yet we don't know where most of the genes are located. By multiple studies we may be able to detect an increase or decrease

in the gene product, thereby being able to eventually relate that particular amount to the extra or missing piece of chromosome material.

Research centers are examining the structure of the chromosome. Cytologic research is being conducted to determine if some chromosomes have a greater likelihood of breaking apart and rearranging themselves to other chromosomes than do others.

Centers are also looking at tissue obtained from spontaneous abortions to determine which chromosomes are most frequently involved in miscarriages and at which stages of fetal development these accidents occur. Most spontaneous abortions due to a chromosome defect occur within the first three months of pregnancy and at least one-third of all spontaneous abortions involve some chromosome error. Therefore, by determining which abnormalities are not compatible with intrauterine development, it can then be discovered which genetic components are most important for viability not only in utero, but also after birth for a long and healthy life.

Parental origin studies of de novo chromosomes are being conducted to determine which parent contributed to the original chromosome error in the hope of establishing better recurrence figures. The reason for this is not to assess fault, but to understand the process of what is occurring in the formation of the egg or sperm that leads to the error. This study has shown preliminary success in determining that the nondisjunction that results in Down's Syndrome is not always maternal as was previously assumed. About 20% of the time the error is found

to be paternal. Down's Syndrome has been used as a prototype for investigations of other chromosome errors.

Epidemiological Field Studies

It has been found that Down's Syndrome children are occasionally born in clusters, clusters that are sometimes geographic and sometimes seasonal. The reason for these apparent "epidemics" is obscure. Epidemiologists who study the frequency and distribution of disease in man are looking at multiple factors in the occurrence of chromosome errors. They collect data regarding parental age, ethnic background, general health and medical history which includes looking at x-ray exposure and drug ingestion before or during early pregnancy. Data are collected on geographic distribution, climate and season of conception. Exposure to environmental toxic pollutants such as pesticides and chemicals is studied. This data on the environmental influence of genetic matter may contribute to answering some of the fearful questions being raised with increasing frequency in the news media.

A Word of Caution

Most genetic research is thoughtful and valid. It is also time consuming and positive results are slow in being obtained. This reality is often difficult for society to accept and when the public presses for immediate solutions to heart breaking problems, there may be answers with premature enthusiasm regarding possible medical breakthrough. Hope, raised by these procedures not yet carefully and scientifically researched, is

brought before the public and laymen, the press, politicians and many others jump on the band wagon of the newest idea. This more often results in disillusionment than in positive progress.

These cautious words do not intend to negate the outstanding work being done in medical research, but are meant to keep in realistic perspective the monumental task of dealing with chromosome disorders.

In any child born with an autosomal chromosome abnormality multiple body systems are involved and mental retardation is a constant component. The cells dealing with the nervous system and brain are the most complex, and it is not realistic to expect dramatic improvement to damage that has existed in the body and mind since the point of, or prior to, conception.

It is in the field of education, appropriate nutrition and medical management of specific handicapping problems that the greatest strides towards improving a child's functioning lies today. The greatest hope for parents dealing with the here and now of their child's handicap is in this area.

CHAPTER VI

PRENATAL DIAGNOSIS

Quote: "I'm not looking forward to going in that day. I guess it is because I have never done it before. It is as much apprehension as anything."

One offer that can be made to a family is an evaluation of the next pregnancy by a procedure commonly referred to as prenatal diagnosis or intrauterine diagnosis. The term amniocentesis means to cut or puncture and is only one part of the whole process. While there are about 80 disorders that can be detected during pregnancy, the ones discussed here will be the chromosome disorders.

PRENATAL DIAGNOSIS IS NOT A PREDICTION FOR THE NEXT BORN, BUT A DETERMINATION OF THE STATUS OF THE CURRENT PREGNANCY. In most instances, amniocentesis and chromosome study offers a family relief from a nine month period of anxiety by allowing them to know that they are not producing another similarly affected child. It does not, however, guarantee a perfect baby. The test is used only to evaluate a specific condition, in this case a chromosome abnormality. There are many other birth defects, such as blindness, heart disease and other causes of mental retardation which cannot be detected prior to birth. However, a high risk family should know of its availability as a procedure, for this procedure with growth of amniotic fluid cells, can detect a chromosome disorder.

Prenatal diagnosis is considered to be safe, though there may be a slight possibility that a miscarriage might occur

following the test. The miscarriage risk in established clinics appears to be less than one percent. This is a risk that is no more than that for the general population who do not have a uterine tap.

Prenatal diagnosis is ideally performed between 15 and 16 weeks of pregnancy. Earlier than the 14th week there is usually insufficient fluid and cells to obtain good studies.

Within the amniotic fluid are the skin cells which have sloughed off from the baby, and it's cells from the baby's mouth, urine and rectum which are grown and processed in the lab. This study takes about the same length of time as a fibroblast study, which is three to four weeks.

Basic steps for amniocentesis at any diagnostic center include:

1. The couple is counseled to make sure the procedures are understood and what risk is involved.
2. A family pedigree is drawn.
3. Ultrasound is accomplished with the gowned woman lying on an examining table with a full bladder. Mineral oil is rubbed on her abdomen to act as a seal for the transducer, which looks like a small upside down microphone head. The transducer is run lightly over her abdomen, transcribing onto an oscilloscope a picture of the baby which can be seen by everyone. This is not a typical bearskin rug photo, but a series of lines in shades of gray which some patients describe as looking like a weather map. The

information given, however, is important. It locates the placenta and the pocket of amniotic fluid. It indicates the gestational size of the fetus and it shows whether or not there are twins.

4. When this information is obtained and recorded, the bladder is emptied and the ultrasound is again applied, this time primarily to locate the pool of amniotic fluid which surrounds the baby. The depth of the fluid within the abdominal cavity is judged and the location of the sack of fluid is marked on the abdomen with a felt pen.
5. The area is then sterilized and shaved if necessary. It is swabbed with iodine. A small area of skin between the naval and public bone may be numbed with a local anesthetic and then a needle is inserted through the skin into the amniotic sac.

   One fear often expressed that can be assuaged prior to the tap is that the procedure is painful. Actually, there is little or minimal pain. There may be a slight sense of pressure or a mild cramping sensation. The whole technique tends to produce more apprehension than pain. Most women describe it as more comfortable than a routine visit to the dentist.
6. About 25cc's or one tablespoon of fluid is withdrawn. The needle is removed and a light sterile compress is applied. This whole process usually lasts less than 15 minutes and the mother is then sent home with instructions to take it easy for the rest of the day.

She is also asked to report any unpleasant side effects immediately.

In the laboratory the fluid, which looks like beer with foam on top, is processed as quickly as possible. This is accomplished by placing the fluid in a test tube, spinning the fluid down in a centrifuge and extracting the cells from the tube. The cells are put in a flask where they adhere to the bottom. The same media that is used for fibroblast studies is then applied and the cells are grown, cultured and harvested just as skin biopsies are prepared.

It takes three to four weeks for cells to grow sufficiently to be examined. However, between five and ten percent of the time the cells in the original sample fail to grow and the woman is requested to return to the clinic for a second procedure. THE FAILURE OF CELLS TO GROW DOES NOT INDICATE ANY CAUSE FOR ALARM AND IS NOT SIGNIFICANT AS TO POSSIBLE PROBLEMS FOR THE BABY.

The results are given to the family as soon as the study is completed. Also, the sex of the baby can be given upon request.

If an abnormality is found, the family is told and the parents can make a choice as to what course of action they wish to take. While specific advice as to what choice should be made is not given, support is given for whatever decision is made by the parents.

CHAPTER VII

THE COMMON PROBLEMS OF BIRTH DEFECTS

Quote: "I thought they were going to tell me she was going to die. That was the very worst thing I could think of."

While individual autosomal defects are rare, birth defects are not. Most birth defects are not familial; however, those resulting from a chromosome abnormality, rather than from another cause, may be familial. While isolation and notoriety may be feelings experienced by a family dealing with a new chromosome syndrome, grief, guilt, anger and anxiety are the universal emotions experienced by any parent dealing with the common problems of cerebral palsy, seizure disorders, mental retardation or physical handicaps.

Babies are all human and dependent individuals with a capacity to grow and develop each in his own way. The nurturing of a handicapped child, while fraught with greater unknowns and fears, has more of the same elements as the nurturing of a normal child than may at first be apparent. The social thrust today for all children is toward normalization, by allowing each child to develop to his optimum capabilities and to live as complete a life as possible within the community as his special needs allow.

This philosophical shift has changed the focus of parental concern. In earlier decades the only option available to a family was institutional placement for their child. Today there are

multiple options available, but each option needs both the support of parents and the commitment of a community behind the parents to make it work.

The increasing willingness of parents over the past thirty years to assume responsibility has resulted in changing medical, educational and social systems, changes that have resulted in enhancing their child's development potential at every age regardless of the severity of the condition. The emphasis lies today not in either "cure" or in "hopelessness," but in "growth."

There is no satisfactory way for a physician or other health professional to tell a family that their child is going to be handicapped. This communication problem is an emotional subject frequently discussed by professionals and parents alike. The parents often criticize the way the problem was dealt with within their family, and the professionals often find themselves on the defensive. The problem is compounded when the physician is unsure if there is a medical concern and, if so, what it is and how serious it will eventually be. There are few anxieties greater for parents to bear than the answer, "I don't know" to the question, "Is my baby all right?" There is a difficult decision to be made as to when it is appropriate to raise parental anxiety and when it is warranted to offer reassurances. Some members of the helping professions have more skill in coping with interpersonal relations at times of crisis than others, and some health facilities have more modern and sensitive methods of dealing with shock and grief, but the final message to the parents is not a good one. There are very few professionals who, within the limits of their training and personality, do not try to do the very best they can

to soften a blow for which there is no real softening possible.

It is normal for a first interview with the doctor to be more emotional than factual. It is normal not to remember what the doctor said during the first interview regarding cause and management.

It is normal to lack self confidence when dealing with new and emotional material. Parents should know that they have certain rights.

1. Parents have the right to feel grief and guilt, anger and anxiety over the problems that have affected their baby. An angry outburst is legitimate. It is not fair; it should not have happened; and life has dealt them a terrible blow.
2. Parents have the right to all of the available medical knowledge about their baby that is appropriate to their situation, and they have the right to expect that the doctors, nurses and social workers are truthful persons.
3. Parents have the right to know of the special needs of their baby and of the problems which they must face and overcome, as well as the right to expect the world to deal with their baby's health as well as its handicap.
4. Parents have the right to demand help from their community, to know and feel free to use the local medical, social, educational and legal resources on which they will have to depend during the various stages of growth of their child.

5. Parents must recognize their own needs, their own limitations and their own strengths. They have the right to time for themselves, for each other and for the rest of the family. Their handicapped child does not have to be the all encompassing center of their universe.

6. Parents have the right to request out of home placement for their child without a sense of guilt or failure. They are the ultimate judge of what is best for their child, best for themselves and best for the others in their family. In spite of the new thrust towards home care, the family home is not always appropriate, and the needs of special children may be best served in specialized medical foster homes, skilled nursing facilities or in institutions.

CHAPTER VIII

RESOURCES WHICH MIGHT HELP

Quote: "After three years I was physically and emotionally exhausted. In three years she had progressed to the age of two months. I could go no further."

There is no one direct source of referral for a family with a handicapped child which will answer all of a family's questions. Unfortunately, today, because the push to obtain services and funding comes from multiple sources, there has been a splintering and fragmenting of local, state and federal programs and a lack of coordination with private and voluntary organizations.

Because every state is so very different, there can be only a generalized description given here of resources that might be available in the community and overall suggestions made as to where to turn for help. For further resources, there is a list of general information sources located at the end of the chapter. For individual state information, a family should contact their State Health Department, their State Department of Education and/or their State Department of Human (or Social) Resources.

Volunteer Organizations

Prior to World War II, help for the handicapped consisted primarily of professionals talking to and writing for each other, about the needs for modern professional and educational services for the handicapped, but no one talked about the needs of the parents, those who carried the primary burden. Parents remained isolated because it was hard for them to bring the problems of their family out into the open and to discuss their own pain and

needs with those whom they feared might not understand. Original volunteer organizations started as occasional and scattered groups who banded together, but still remained isolated one from the other.

In the 1950's, communication began to spread and it was discovered that among other important things, the sharing of common problems, needs and experiences helped heal parents' wounds. The effect of these early parent organizations was to provide a source of mutual aid and comfort, a basis for direct action in obtaining better opportunities and treatment for their own children, as well as to act as an agent in bringing about broad changes in social and public policy. The evolution of volunteer organizations has grown from fragmented attempts to change local injustices to large national organizations with recognized economic and legislative power.

A forerunner and prototype of a successful national group which has grown from grass roots efforts to national scope while retaining its local focus has been the Association for Retarded Citizens. Today, this organization has a total membership of over 218,000 with more than 1,700 state and local units encompassing all types of communities, both metropolitan and rural. The thrust of energy within the ARC group has been to assure appropriate educational opportunity, appropriate vocational training and appropriate living facilities for each mentally retarded person while also giving emotional support to their families.

While it has had a profound impact at state and national levels to implement change, to modify public attitudes and to

stimulate professional attention to unmet needs, it has, at its heart, remained a local group run primarily by parents and has remained committed to local need.

Parent Groups

Parent groups are either involved in isolated local efforts, are units within national volunteer organizations, or are groups organized through County Mental Health Clinics, hospitals or counseling centers. There are as many possibilities for parent groups as there are communities and they often reflect an unmet need within the community. The focus of these groups is usually to achieve a goal or to render a service. Three general areas of focus for groups are service, parent education and advocacy. Some examples are:

1. Service Groups

Parent to parent counseling is a group process conducted as a service. Usually it is offered by experienced and trained parents of developmentally delayed children who "have been there" and who are willing to counsel families with a newly diagnosed handicapped child. These groups are becoming successful. It has been found that parents who have already been over the ground that new parents are currently covering can give a sense of perspective and hope to a new family which is difficult for a professional to convey.

2. Education Groups

Parent education groups are often originated by agencies and are run by medical social workers, counselors or other health

professionals. These groups allow parents, within the warmth and support of a group, to absorb vastly complex and emotionally laden medical information on both an intellectual and emotional level, thereby helping them reduce the impact of their child's handicap to manageable terms. These groups are usually time limited and are fairly specific in content and structure, but may be the nucleus for continuing friendships or for forming other groups.

3. Advocacy Groups

Early childhood education for the handicapped has resulted in increased independence, increased social skills and increased developmental skills with the ultimate result that handicapped children are able to fit more appropriately into the public school programs that are being developed for their special needs. This demand for quality education begins in the newborn period and parents of these preschoolers by raising their voices have been instrumental in developing excellent programs for their children within their community. Because of the advocacy of these parents, state universities, colleges of education, and special training centers are graduating skilled professionals in the field of special education and related subjects, graduates whose purpose today is to enhance the early childhood experience of all young children, including the physically and mentally needy.

Public Organizations

Publicly funded programs vary from state to state and within communities. In the past fifteen years, state government

expenditures in the areas of public welfare, education and human services have increased at a greater rate than the expenditure of the federal government. As a result, states are now attempting to coordinate and manage the many developmental disabilities programs that have evolved locally but are funded from both local and federal sources. The most common trend is towards one umbrella state human services agency which is responsible for the planning, coordination and administration of all health, mental health, and general welfare services.

All states should have services which include, at a minimum, the following:

1. COUNTY HEALTH DEPARTMENTS should be able to provide public health nurses and well baby services for families while also serving as a referral source for more specialized medical care.
2. COUNTY MENTAL HEALTH CLINICS should have counseling services available to any person or family, regardless of income, who need help in dealing with the emotional components of their child's diagnosis.
3. CRIPPLED CHILDREN'S SERVICES should offer financial services for specific crippling conditions. The financial and medical criteria for service covered varies from state to state.
4. SPECIAL EDUCATION should be available through local school districts or state departments of education for any child with special educational needs.
5. PUBLIC WELFARE is available as a financial help for families. In many instances, it is also the resource for obtaining funding for institutional placement or

other out of the home care.

Education for the Handicapped

In 1933 a group of five mothers in Ohio banded together in an "indignation meeting" because their handicapped children had been excluded from the public schools. Out of this protest came the formation of a special class sponsored by the parents themselves to serve excluded children.

Public Law 94-142, the Education for All Handicapped Children Act, was passed by the 94th Congress in November, 1975. It assured a free appropriate public education for every handicapped child by 1978. This law is a culmination of the work of these parents, and other like them, who struggled to provide equal educational opportunities for their handicapped children. The Act is designed to meet the needs of children from ages three to twenty one, the purpose being to help each handicapped child become all that he or she is capable of becoming.

The Act defines special education to mean specifically designed instruction to meet specific needs and it may include placement in a special class, or the design of a special program to be carried out in a regular classroom. It may mean home instruction or classes for children in hospitals, state schools or institutions. It includes related services to aid in the implementation of the educational program, such as transportation, physical and occupational therapy, medical and counseling services.

To determine if a state participates in the Education for All Handicapped Children Act, inquiries should be directed to the local school superintendent or to the State Department of Education.

Supplemental Security Income

Children of any age who are disabled may be eligible for monthly cash payments from the Federal government. These payments, called SSI, are made to persons, or in the case of minors, the parents of persons, who are unable to engage in gainful activity because of physical or mental impairment and whose parents have little or no regular income and very limited assets.

The Social Security Administration runs the SSI program, but SSI is not the same as Social Security benefits. Money for SSI payments comes from general funds of the U.S. Treasury, while Social Security benefits are paid from contributions of employees, employers and the self-employed.

To determine if a handicapped child is eligible for SSI, parents should contact the Social Security office closest to their home.

Alternatives to Home Living

The social thrust today for all children is towards normalization. Each child should be encouraged and allowed to develop to his optimum capability and according to his own capabilities and needs. As noted before, parents have assumed greater responsibilities in the past thirty years in obtaining this goal. A more nearly normal family cycle in the child's development from the dependency of childhood, growth, maturation, to departure now results even for those whose pattern of development varies from the norm.

Parents cannot always keep their children at home since it is not always practical, feasible or possible. Nevertheless parents often feel guilt at having to make other arrangements

for their special child. As a consequence, parents sometimes need encouragement to let go and accept the fact that there are equally good alternatives to their own home. All children must leave to grow whether it be temporarily as a child or permanently as an adult. Parents, by allowing children to leave at appropriate times also enhance their own growth.

Communities today are trying hard to develop alternative plans for children and families, plans which will in each individual situation be the most appropriate for that child's care, welfare and growth.

1. RESPITE CARE is temporary care offered to a family for the care of their child by others. It can range from the care given by a trusted babysitter to temporary institutional placement. It can be used for emergencies, by prior arrangement for family vacations with the other children, or on a regularly scheduled basis for relief. Unfortunately respite care is not available as frequently as is needed. Some state agencies offer the service to families through their foster care plan, or sometimes there are programs that are funded through the health department or through developmental disabilities programs. Usually those families providing relief care are trained in the handling of special needs and are under the supervision of a responsible agency. Respite care is a superb alternative for the family who wishes to have their child remain in the home indefinitely, but also needs temporary relief from the full-time responsibility of care.

2. FOSTER CARE is a viable alternative between being raised in the parents' home or being placed in an institution. Many children demand more care than one family can give, but with special help can remain in the community. Foster care, offered by state or private agencies, can be either temporary or permanent and is particularly successful when parents wish the child to remain close to them within their community, but who cannot maintain the child full-time in their own home. The decision of parents to place a child in foster care shows a parent's ability to share and to trust another. A major step towards growth is in the ability to let go and to allow a second family to be a part of their child's life.
3. EXTENDED LIVING or GROUP CARE is the resource currently being developed for the young adult who will need lifetime supervision, but who can enjoy some degree of independence. The expectation for group care for a handicapped individual follows the normal life cycle of the family who expects their children to grow, mature and leave home. The variation from normal for this situation is that instead of a job or marriage, the young adult will enter a supervised living arrangement such as special apartment complexes, board and room arrangements or a mini institution. Along with this they will have available a protected job or activity that is within their capacity. In this way life will consist of independence as well as protection.

4. STATE or PRIVATE INSTITUTIONS offer long-term care to the physically and mentally handicapped. Unfortunately the word "institution" has developed a poor reputation in recent years, conjuring up visions of impersonal warehouses, storing preferably forgotten products. There is absolutely no necessity for this picture to be true. There is a time and place for an institution, one that has at its disposal appropriate medical and educational staff as well as therapists and social workers. Any family should feel comfortable in applying for institutional care for their child and in demanding that the care be optimal. Attentive life-long care in an institution is possible for anyone who has an advocate in the form of a family or surrogate family who will remain involved and make their demands for quality care known.

INFORMATION SOURCES

American Association for the Education of the Severely and Profoundly Handicapped
1600 W. Armory Way
Seattle, WA 98119

American Genetic Association
1028 Connecticut Avenue
Washington, D.C. 20036

Closer Look: National Information Center for the Handicapped
Box 1492
Washington, D.C. 20013

Council for Exceptional Children
1920 Association Drive
Reston, VA 22091

Epilepsy Foundation of America
1828 L Street NW
Washington, D.C. 20036

Federal Programs Information and Assistance Project
1522 K Street, NW, Suite 1030
Washington, D.C. 20005

Joseph P. Kennedy, Jr. Foundation
1701 K Street, NW, Suite 205
Washington, D.C. 20006

National Association for Retarded Citizens
2709 Avenue E East
Arlington, TX 76011

National Clearinghouse for Human Genetic Diseases
1776 East Jefferson St.
Rockville, MD 20852
(301) 279-4642 or 4643

National Clearinghouse of Mental Health Information
Public Inquiries Information
5600 Fishers Lane
Rockville, MD 20857

National Education Association
1201 16th Street, NW
Washington, D.C. 20036

National Genetics Foundation
9 West 57th Street
New York, NY 10019

National Institute of Mental Health
Public Inquiries Section
5600 Fishers Lane
Rockville, MD 20857

Parenting Materials Information Center
S.W. Educational Development Lab.
211 East 7th Street
Austin, TX 78701

The National Foundation, March of Dimes
Box 2000
White Plains, NY 10602

United Cerebral Palsy Association
66 E. 34th Street
New York, NY 10016

CHAPTER IX

CANDID CAMERA

Photos of Children at Home and in School

Children with chromosome abnormalities fit into their world more easily than originally expected. The criticism of the following photographs has been that the children are "too cute," therefore not being representative of the typical chromosomally abnormal child. It was impossible to find children who were not "cute" because they all reflect the same qualities; they are well cared for, loved and busy.

LEARNING TO NAVIGATE - ONE STEP AT A TIME

First comes the safety of the parellel bars.

Next there is encouragement and support from the physical therapist.

She is on her own!!! How proud they both are.

He is developing even greater mobility. Concentration and hard work bring new independence to the previously floor bound child.

The task is hard. One block at a time is carefully placed.

It is getting easier. He is going more rapidly now. Careful records are kept to track each child's progress.

The teacher both verbally and with her hands clearly communicates "correct." Another skill, this one in communication, is being conquered.

DEVELOPING SELF HELP SKILLS-ON THE ROAD TO GROWTH

A time for lunch offers training in socialization skills, fine motor coordination and communication. Teachers don't miss an opportunity to use this time to further the learning process.

ACTIVITIES ARE ROBUST - AT HOME AND IN THE NEIGHBORHOOD

Lots of roughhouse and outdoor play builds big muscles and develops a sense of well being.

Little brother offers competition and companionship. Look out neighborhood, here we come!

IT IS A BIG WORLD - AND AN EXCITING ONE

Large play equipment offers a challenge to explore. What a sense of pride when she has reached the top!

CHAPTER X

TALKING WITH PARENTS

As the chapter quotes show so well, no one can speak for parents as well as they can speak for themselves. The following vignettes are condensations of interviews with mothers who have, through time, hard work, tears and determination, come to an acceptance of reality in dealing with the emotional impact of giving birth to a child with a chromosomal abnormality. They agreed to the interviews, which were occasionally painful, with the hope that they would be of help to others who are also dealing with the same problems they have experienced by letting them know they are not alone.

The Time of Diagnosis

Traci is almost six years old and attending classes for the Trainable Mentally Retarded in the public schools. She does not yet walk or talk.

Traci was our third baby and we finally got our girl. Looking back now I wonder how I could ever have been so blind, but I was. We went in for regular check-ups and the doctor never said much. He was quiet and would say things like, "Let's see how she does next month." I didn't see a problem; I was the last to know. She was such a good baby. She never cried much, of all three she was the easiest to care for. She wasn't doing things like rolling over, but I thought she was just a little slower.

My mother knew something was wrong and she called the doctor.

He told her to come in with me for our next check-up. We went into the doctor. It was a Friday. It was in September. I guess you don't forget days like that. The doctor asked if Traci was doing anything new and I said, "No."

"I definitely feel there is a problem here," he continued.

"What do you mean?" I was so shocked; it was stupid to be shocked, but I was . . . completely shocked.

"I think Traci will be retarded. She will probably never learn to read." I remember thinking that was a stupid thing to say about a six month old child. I started to cry. That's how I usually handle things; it was all I could do.

It was my mother who suggested the Genetics Clinic. I had never heard of it, but the doctor agreed because he really didn't know what the problem was. He said he'd refer us.

We went home. I remember my father-in-law was there. You really remember days like that; they stand out in your mind. My mother told my husband Traci was retarded. He was very angry; he thought the doctor should have at least warned him of his suspicions. I told him the doctor wasn't sure at first. Maybe he hadn't been sure, but I wish he'd leveled with me earlier and not let it go on for so long.

My husband put Traci down for her nap and I went in to lie down. It was horrible, just horrible. Pretty soon he brought Traci to me and said, "Your daughter doesn't want to sleep. She wants to be with you."

It was good when I held her. I wondered, "Why us? Why not someone who wouldn't care so much?" I had never been around a

handicapped person; I'd never noticed a retarded person. There was no one in the world less prepared to cope than I. I was frightened of it all. For three months it was like that, really bad.

It took three months for the diagnosis. Those were the hardest times of all, those three months. Up until then we didn't suspect there was anything wrong and after that we were told there was something the matter, but we didn't know what it was and we were getting no answers, no satisfaction and no help. We were in limbo; it was horrible.

We didn't want to go out for awhile. Our friends knew; they knew even though we hadn't said anything. I remember we were invited to a party and I said, "No."

"Yes, you are going to come," said my friend who had a baby the same age as Traci. We went. I didn't know what I was going to say, but it was good that I was forced into that party because it wasn't so hard after that. Then we began to talk about it. Our friends were really interested and it helped to talk about it.

The doctors were nice. In fact they are now my good friends, but it was hard when there were no easy answers. It took two or three trips to the clinic before we got the answer that Traci had an unusual chromosome translocation. That didn't mean much to me. It still doesn't mean a lot. I think probably way down deep I still don't believe that a tiny little particle should make such a difference to her.

After we got the report from the Genetics Clinic, even though it was foreign and hard to understand, we started to put our life

together. We could do things again. Until then, that year was lost, but at least from then on we had something to go on.

Even though we weren't offered a cure, we were offered help. Traci started seeing a physical therapist once a week and it was as much therapy for me as it was for her. At least I was doing something for her. It hasn't been clear sailing. There is support, but you have to seek things out for yourself. She has gone from therapy to a preschool. Next year she will be six and we are looking into the right school program for her. We don't plan too far ahead. Six years ago I couldn't believe we would be where we are today. We take each day as it comes.

On Carrying A Familial Translocation

Cindy's mother carries a balanced translocation which she passed on in the balanced form to one daughter and in the unbalanced form to another daughter. After three years of severe medical problems, the baby died in a child care center.

I had an advantage over my sisters because when I was pregnant, I didn't know what I was facing with each pregnancy as I and my sisters do now.

When I was sixteen, my older sister's baby died at age three with what they called cerebral palsy. I helped take care of her, but later didn't think a lot about her until I was pregnant with my first baby and started wondering if I would have a baby with cerebral palsy, too. I think every mother kind of runs that through her mind. I think it is normal. My doctor said just because my sister had a baby with cerebral palsy was no reason I would. It wasn't hereditary.

I had my first two babies with no problems, but when Cindy was born and they put her in my arms, I knew something was wrong. She was too little and too weak; she wouldn't nurse. The nurse kept saying things like, "Well, you know how these little ones are," but I knew something was wrong, even though I couldn't put my finger on it.

Now, I know subconsciously I was saying to myself, "Hey, this one feels like Donna's baby, limp in my arms."

For four months everyone kept saying, "Nonsense, nonsense, there's nothing wrong." At four months I told the doctor he had to tell me what was wrong and he agreed something was, but he didn't know what. It was time for a specialist and we were sent to the medical school. For four more months we looked for answers. When they said it was chromosomal, I knew that it was on my side of the family and that I was a carrier. Call it instinct, but after having cared for my three babies and my sister's baby, I just knew. While it came as no surprise, I still didn't feel anything for a while. I was numb. They only confirmed what I already knew, but I was still numb. It is one of those things that you don't want to believe even while you are knowing it. It has to grow on you I think.

During those next months I never stopped running. I was in perpetual motion. I knew if I ever stopped I would never start. I thought just as hard as I ran, and when I finally slowed down and faced the ralization of what I had to face and deal with, I cried. I cried a lot. Finally I remember thinking, "Hey, this is getting me nowhere; I am just standing still." Somewhere about then I started to pull myself together and to progress one

day at a time.

One thing we never did. We never hid the facts from the other kids. We sat them down each time after every clinic visit and told them what we understood the doctor had said. Some things probably went over their heads, but we wanted things in the open.

Having the blood drawn on the children was more traumatic for them than the reason behind it. When we got the results back and found that our oldest daughter was a carrier too, it wasn't too hard to tell her because she was too young to really understand, to put it into perspective. It is now that she is older that she has to face it. Now she doesn't want to talk about it.

My father was dead and my mother's chromosomes were normal. He was the last living of his brothers and sisters. I have a lot of first cousins and they all eventually had their blood drawn, I think. When I called them, I didn't try to really explain what was going on; I told them the doctor would. He called some and wrote to those who lived far away. All checked out normal; none had a problem. They had to find out the results for themselves. For their children's sake it was important to them, but after the first reaction of, "What?," I never had anybody on either side of the family come back on me and we've never talked about it since.

My younger sister was sixteen when our family was studied. She is a carrier too. She was going with the fellow she married; he was sixteen, too. They were just kids then, but I've been very proud of Ken. I don't know how many men could have handled the

news that well and say, "Hey, it's our problem." He's always been great.

I don't think I could have faced another pregnancy. If I had ever found out that I was going to have another child like Cindy, I don't think I could have dealt with it. Even now, knowing what it did to the family, I couldn't ask them to go through it again; I couldn't go through it again. I still have moments, flashbacks. I could dwell on those years, but I don't.

Asking for Help

Kay has been living in foster care for eight months. Her parents retain legal custody and are financially responsible for her care.

Even before Kay was diagnosed we knew her problems were going to be serious and no Band-Aid was going to help her, but the hardest thing in dealing with her chromosome abnormality was in the not knowing what to expect next. The first thing we wanted to know was what did it all mean? There were so few other children like her. What was going to happen to her? What was she going to be like? When you can't get those answers right away, it leaves you so lost. You just can't really believe that doctors don't know everything. It takes a long time to deal with the unknown and put it into perspective.

We knew raising Kay was not going to be like raising a normal child you prepare for the world. She was infantile and she always would be. We knew she would have to be watched every minute and not left alone for a second. She is almost blind;

she has no judgment and she is almost fearless. Even when she hurts herself she doesn't know what she has done. I had visions of being sixty years old and still having this adult infant on my hands. I had to ask myself, "Can I deal with that?" I didn't think I could.

We had to deal with her now, the finality of her and the fact that we weren't going to change her. At times it was so hopeless we were almost in despair, but at other times we told ourselves to knock it off and face it as it was. We had to continue our lives, to make a plan for Kay and for ourselves. Our lives came to a standstill while we debated what to do.

We talked about foster care, but it really bothered me at first. I always thought I was the kind of person who could handle just about anything, and then when I found out I couldn't, it really shook me. It really tests your self-esteem. The first thing you have to ask yourself is, "Why can't I handle this? Am I a good mother if I can let someone else take her?" I care about being a good person, a good mother, a good person to my friends, a good wife; I really care about those things. I think I am a good person; it is in the caring and trying that counts.

We decided to talk to the state about foster care. A worker came to our home and right away said that Kay would fit into their program as soon as we were ready for it. We decided if we were going to make a decision like that we couldn't mull it over and over. We decided to try it to see how it would work, knowing we could always take her back. It was a relief to have the Browns say they would take her.

Kay is in temporary foster care. We have legal custody; the state does not. She receives SSI and we pay the state the difference for her care. We feel we have done the right thing. The Browns are trained in the care of handicapped children and are licensed by the state as medical foster parents.

At first it bothered me to see Kay in someone else's home and then it bothered me because it didn't. Now I know that it really takes two families to raise a child like Kay. She lives in a little protected circle. She has the Browns and she has us. Her foster parents are older than we are and she loves her daddy and her grandpa Brown the best. We take her one or two days a week when they need a rest. We know the Browns love her and they know we love her; we are both free to love her. We are awfully lucky to have the Browns; I don't know if there are many families like that.

It is hard to plan too far ahead. They will keep her two more years and then we don't know. Right now we don't even plan a week ahead. For now we will leave things as they are. Kay is happy where she is; she has them and she has us. Our life is no longer at a standstill.

Breaking Away

Anne was placed in the state institution when she was ten. She is now fourteen.

Hope, that is a hard one. I remember one doctor said, "You have a very special child here. We can repair many things today, but when the problem affects the brain, there is nothing we can

do about it." We were told to take Anne home and treat her as we would a normal baby. At that time, science didn't know any more about her than we did.

As Anne grew older we vaguely knew we would have to someday consider an institution. We explored resources and tried as many shots in the dark as most parents. At first everything seemed such a hassle and we were never really satisfied. We felt we could cope and care for her as well as any institution so we kept her at home.

Things changed and the question became, "How could I go to work and handle her at home at the same time?" The vague idea of placing her sometime in the future became a reality. You have to be realistic. Even with good school programs you have to think what the home can provide. You have to know how far you can extend yourself so we applied for admission to the state institution and took her there when she was ten.

After ten years of living at home as a close family group, it was a hard break to make. The very hardest adjustment was missing her physical love. She didn't walk so we always carried her and held her and we found we missed her hugging and kissing that went with it.

Anne missed the physical love too. At first she was ill a lot, and she was returned home to our hospital each time. That was great for her and it made me happy too, having her that close, but it became apparent that her constant returns were helping neither of us. It was the psychiatrist who helped me understand her problem was infantile depression and that her

returns home were making her health worse. They started keeping her there and eventually her health stabilized.

It is funny, but now she is happier at Fairview than she is at home. I didn't think I could ever say that. She has her friends and her family is now 45 in size. At home she is lonely. She doesn't say "Mama" anymore; it is no longer part of her vocabulary, but she knows the children in her program and it is they who will be her friends for the rest of her life.

It is easier to visit her now. Time has helped. She is still learning, for which we are grateful. The staff know me and have been of great help by showing me her school records and telling me about her progress. They know we care.

It is still hard not to just snatch her and run to the car and run away and never go home, but you bring yourself back to reality and you do what you have to do.

GLOSSARY

ACENTRIC FRAGMENT: A small section of chromosome which does not contain a centromere (constriction).

ACROCENTRIC CHROMOSOME: A chromosome in which the centromere's location creates an extremely short short arm.

AMNIOCENTESIS: (To cut or puncture) The procedure used to extract the amniotic fluid from the uterus.

ANIRIDIA: Absence of the iris of the eye.

AUTOSOMAL CHROMOSOME ABNORMALITY: A chromosome abnormality involving one of the 22 pairs of autosomes, those chromosomes which do not play a role in sex differentiation.

AUTOSOMES: The 22 chromosomes found in each cell which hold the genetic material responsible for the individual characteristics in each person which do not play a role in sex discrimination.

BALANCED TRANSLOCATION: A rearrangement translocation with no loss or gain of chromosome material, resulting in a clinically normal, but genetically abnormal person.

BANDING PATTERN: The pattern of bands found on each chromosome.

BANDING TECHNIQUE: A laboratory expression referring to the procedures used in uncovering bands on chromosomes.

BONE MARROW: The soft organic material that fills the cavities of the bones.

CAT CRY SYNDROME: Also called Cri du Chat or 5p-Syndrome, resulting in the absence of the terminal end of the short arm of chromosome number 5.

CELLS: Individual units of living protoplasm each containing a nucleus and held together by a cell membrane.

CENTRIC FRAGMENT: A small section of chromosome which contains a centromere.

CENTROMERE: The point where the dividing chromosomes are temporarily held together prior to splitting and going into new cells.

CHROMOSOMES: The thin rod-like fibers of material in the nucleus of each cell which contain the genes which give each person his or her individual characteristics.

CONGENITAL: Present since birth.

CRI DU CHAT: Cat Cry or 5-p Syndrome.

CROSSING OVER: A sequence in meiosis in which some maternal chromosome material and some paternal chromosome material exchange material.

CYTOGENETICS LABORATORY: A laboratory specializing in determining chromosome abnormalities.

DAUGHTER CELLS: The term used for the two new cells created from the one original cell.

DELETIONS: Chromosomes that have had a piece broken off which has disappeared.

DE NOVO TRANSLOCATION: A translocation which is the result of an isolated incident where both parents are found to be chromosomally normal.

DERMATOGLYPHICS: The study of the fine ridge patterns found on the fingers, palms and soles of the feet.

DOWN'S SYNDROME: Trisomy 21 (previously called Mongolism).

DYSMORPHIC: A collection of abnormal external features usually seen in the head, hands and face which may be indicators of more serious internal problems.

FAMILIAL TRANSLOCATION: A chromosome rearrangement that has been detected in more than one family member and has been demonstrated by clinical study or by inference to be inherited.

FAMILY TREE: A diagram of family relationships.

FIBROBLAST: Cells grown from skin tissue or amniotic fluid.

FRAGMENT: A small piece of chromosome material which may or may not be significant.

GAMETES: A female or male germ cell which, when joined by the opposite sex cell, results in reproduction.

GAMETEGENESIS: The occurrence in which cells reduce from 46 count chromosome cells into 23 count chromosome cells, one of each pair.

GENES: Inherited units of molecules which code for each person's specific characteristics.

GENETIC DISEASES: Abnormalities caused by single genes, several genes, or by excess, deficiency or rearrangement of the chromosomes which may influence a large number of genes.

GENETICS: The branch of biology which deals with heredity.

GIEMSA BANDING: A commonly used technique for chromosomes which allows many individual bands to be easily seen.

HOMOLOGUES: The 23 matching pairs of chromosomes.

HUMAN GENETICS: The study of those traits, good or bad, that are passed on from parents to children through succeeding generations.

HYPERTELORISM: Widely-spaced eyes.

IDEOGRAM: A stylized standard diagram of chromosomes arranged by length and banding patterns, first established at the Paris Conference, 1971, and now being revised as new bands are being uncovered.

ILIAC CREST: Top of the hip bone.

INTERSTITIAL DELETION: A segment of chromosome is cut out, not including the end. It involves two breaks in the chromosome.

INTRAUTERINE DIAGNOSIS: A diagnosis made on the unborn usually following the procedure referred to as amniocentesis.

INVERSION: The result of two breaks occurring simultaneously in the same chromosome with the free segment turning upside down before being reinserted and repaired.

ISOCHROMOSOME: A chromosome which is thought to split horizontally instead of vertically, resulting in an individual who has only a single copy of one arm of a chromosome and three copies of the other arm.

KARYOTYPE: An enlarged photograph of a cell containing the chromosomes that have been cut out and arranged on a sheet of paper according to their size and banding pattern.

KLINEFELTER'S SYNDROME: A male who has two X chromosomes and one Y chromosome, resulting in a 47, XXY karyotype.

LARYNX: The area of the throat containing the vocal cords.

LYMPHOCYTES: A specific type of white blood cell from which chromosomes are obtained in blood cultures.

LONG ARM: The bottom half of the chromosome below the centromere.

MACROCEPHALIC: A head that is proportionately too large for a person's height and weight.

MEDICAL GENETICS: The branch of medicine that deals with disorders which are inherited.

MEIOSIS: The process of reduction of 46 count cells to 23 count cells prior to fertilization.

MENDELIAN INHERITANCE: The inheritance of single gene traits that are passed on from parent to child in a specifically prescribed manner.

METACENTRIC CHROMOSOME: A chromosome in which the centromere is approximately in the middle.

METAPHASE: The chromosome reproduction phase just prior to the chromosome separating where the chromosome becomes temporarily short and puffy and the two halves are held to one another at approximately the middle.

MICROCEPHALIC: A head that is proportionately too small for a person's height and weight.

MITOSIS: The process of cell division in which the chromosome first makes a copy of itself and then separates, each copy going into a new cell.

MONOSOMY: A cell in which there is only one copy of a chromosome instead of the accurate number of two chromosome copies.

MOSAICISM: At least two distinct cell populations, most commonly one cell population having a normal complement of 46 chromocomes and the other having a 47 chromosome count.

MULTIFACTORIAL: Many factors. The interaction of several genes with the influence of the environment.

MULTIPLE CONGENITAL ANOMALIES: Several physical and/or developmental problems present since birth.

NONDISJUNCTION: An occurrence when chromosomes fail to separate or disjoin properly and go into separate cells during first or second meiosis, causing one cell to have two copies of a chromosome and the other cell none.

NUCLEUS: The center protion of each cell which is the control center for that particular cell and which contains the chromosomes.

p SEGMENT: The short arm of the chromosome.

PARACENTRIC INVERSION: An inversion that does not include the centromere.

PATELLA: The knee cap.

PEDIGREE: A genetic and medical history of a family covering at least three generations.

PERICENTRIC INVERSION: An inversion involving the centromere.

POLYGENIC: The influence of many genes.

PRENATAL DIAGNOSIS: A diagnosis made on the unborn, usually by the procedure referred to as amniocentesis.

PROTOPLASM: Living materal.

q SEGMENT: The long arm of the chromosome.

RANDOM SEGREGATION: The 50% chance during meiosis as to whether the maternal or paternal chromosome enters each new cell.

RING CHROMOSOME: A chromosome where both ends have broken off and the raw ends have adhered to each other creating a ring.

SATELLITE: The small segment of material found above the stalk on acrocentric chromosomes.

SEX CELLS: The germ cells, either the sperm or the egg.

SEX CHROMOSOMES: The two chromosomes, found in each cell responsible for the male and female characteristics; XX representing the female and XY the male.

SHORT ARM: The top half of the chromosome above the centromere.

SPERMIOGENESIS: The process which results in the production of sperm.

SPONTANEOUS ABORTION: An accidental interruption of pregnancy, usually before the 21st week.

STALK: The almost unseen area of the chromosome between the terminal end of the short arm of the acrocentric chromosome and the satellite material.

STERNUM: The breast bone.

STILL BIRTH: The birth of a dead child.

SUBMETACENTRIC CHROMOSOME: A chromosome in which the centromere causes the short arm of the chromosome to appear distinctly shorter than the long arm.

SYNDROME: A total collection or pattern of symptoms that can result in a distinct clinical diagnosis.

TERMINAL DELETION: A section from the end of the chromosome is missing.

TIBIA: The shinbone.

TRANSLOCATION: A chromosome rearrangement involving exchanges between two or more different chromosomes.

TRISOMY: A cell in which one chromosome has three copies of itself instead of the accurate number of two chromosome copies.

TRISOMY 21: Down's Syndrome, a common birth defect in which there are 47 chromosomes in each cell instead of 46, the extra chromosome being the number 21.

TURNER'S SYNDROME: A female who has one missing or malformed X chromosome, resulting in short stature and infertility.

UNBALANCED TRANSLOCATION: A translocation with loss or gain of chromosomal material resulting in a clinically and genetically abnormal person.

WILM'S TUMOR: A malignant tumor of the kidney occurring during early childhood.

ZYGOTE: The combined egg and sperm from conception to about the tenth day of conception.

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